TO STUDY THE EFFECT OF ANTIEPILEPTIC DRUGS ON MIGRAINE IN PATIENTS WITH NEW ONSET EPILEPSY

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Dedicated

to

my Family

&

Teachers

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Dr. Samriti Jain

ABBREVIATIONS

ADR	Adverse Drug Reaction
AEDs	Antiepileptic Drugs
AEs	Adverse Events
AMPA	Alpha Amino-3-Hyroxy-5-Methyl-4-Isoxazole Propionic Acid
ANTI 5-HT	Anti-Serotonergic
BRV	Brivaracetam
CBZ	Carbamazepine
CNS	Central Nervous System
CPS	Complex Partial Seizures
CRMP -2	Collapsin Response Mediator Protein-2
CSD	Cortical Spreading Depression
EEG	Electroencephalograph
FHM	Familial Hemiplegic Migraine
FHM 2	Familial Hemiplegic Migraine Type 2
FHM1	Familial Hemiplegic Migraine Type 1
FMH 3	Familial Hemiplegic Migraine Type 3
fMRI	Functional Magnetic Resonance Imaging
GABA-A	Gamma Amino Butyric Acid – A
GAMS	Global Assessment Of Migraine Severity
GASE	Global Assessment Of Severity In Epilepsy
GTCS	Generalized Tonic Clonic Seizures
ICHD-3	International Classification Of Headache Disorders – 3
ILAE	International League Against Epilepsy
LAC	Lacosamide
LEV	Levetiracetam
LTG	Lamotrigine
NO	Nitric Oxide
NSAIDS	Non Steroidal Anti-Inflammatory Drugs
OXC	Oxcarbamazepine
PB	Phenobarbital

PHT	Phenytoin
PWE	Patients With Epilepsy
SHM	Sporadic Hemiplegic Migraine
SPS	Simple Partial Seizures
SPSS	Statistical Package For The Social Science
TCAs	Tricyclic Antidepressants
TPA	Topiramate

ABSTRACT

Introduction: Epilepsy is characterized by unprovoked seizures that require long term or lifelong therapy. Antiepileptic drugs are the main stay for treatment of epilepsy. AEDs are known to have additional effects in comorbidities mainly migraine. It is seen that epilepsy is associated with migraine but is often under recognized. Migraine is characterized by recurrent headaches often accompanied by photophobia, phonophobia and nausea. There are several clinical features which are observed to be common between epilepsy and migraine, this gives a clue to their pathological overlap. FDA has approved few AEDs as a prophylactic treatment in migraine.

Aim and Objectives: To study the frequency of migraine in patients with new onset epilepsy and to study the effect of various AEDs on frequency, severity, pattern and disability in patients of migraine.

Methods: Patients suffering from epilepsy and migraine who were on AEDs monotherapy on stable dose (3 months) were recruited from the neurology and epilepsy OPD after prior approval from institutional ethic committee. Follow up was done for three months after dose stabilization. Patients were asked to maintain a migraine dairy to record the frequency of migraine attacks per month. Severity of migraine attack was assessed by using VAS and GAMS scale. A questionnaire regarding the headache was filled at the time of enrollment. Demographics of the patients were filled in a pre structured performa.

Results: In this study of 102 patients, predominant age group was 21-40 years. Stress (46.1%) followed by exposure to sunlight (37.3%) were the most common triggering factors for migraine along with many others. Majority of patients were of GTCS (51). Significant decrease in frequency and severity was seen with VPA and LEV (15-20mg/kg). LEV (8mg/kg), OXC and LAC also showed promising results.

Conclusion: Based on the results, it was found that AEDs like LEV and VPA showed significant decrease in migraine frequency and severity. The effect of AEDs was augmented with propranolol in reducing frequency and severity of migraine (with or without aura).

Keywords: AEDs, Migraine, VAS, GAMS

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INTRODUCTION

Epilepsy is the most common neuronal disorder after stroke and is characterized by presence of recurrent seizures due to chronic underlying process. The incidence of epilepsy is ~0.3–0.5% in different populations throughout the world, and the prevalence of epilepsy has been estimated to be 5–10 persons per 1000 population. Epilepsy is characterized by unprovoked seizures that require long term or lifelong therapy.[1]

Seizure is the transient alteration of behaviour because of disordered, rhythmic and synchronous firing of brain neurons whereas epilepsy is periodic and unpredictable occurrence of seizures due to brain function disorder. Seizures lead to transient impairment of awareness and individuals suffering from seizures are at risk of bodily harm; it also interferes with their education and employment [2]

International League Against Epilepsy (ILAE) had last classified epilepsy in 2017 with unknown onset, which includes seizure types as tonic-clonic, atonic, and epileptic spasms in order to understand epilepsies and their underlying mechanisms. [3]

Majority of the people with epilepsy are treated with antiepileptic drugs (AEDs) and approximately 70% undergo remission once the most effective regimen is followed. [4] AEDs are the mainstay for treatment of epilepsy and most of the patients suffering from it achieve good control with medicines alone. Newer drugs with novel mode of action have improved safety profile. [2]

AEDs are known to have additional effects in comorbidities mainly migraine, neuropathic pain etc. [5] It is seen that headache is associated with epilepsy but it is often under recognized and as a result it is often under-treated. Worldwide, about 46% of population has active headache disorder. Migraine represents about 11% among them.[6]

Migraine is characterized by recurrent headaches with moderate to severe intensity often accompanied by photophobia, phonophobia, and nausea. It can aggravate with physical activity, is often unilateral but can be bilateral as well. The headache may have a throbbing, pulsating or

burning character.[7] The underlying pathophysiology of migraine is not well understood till date. It is assumed that malfunctioning of brain areas and channels, which modulate the excitability of nociceptive brain circuits and central sensitization may play role.[7] Studies have found that migraine occurs along with other co-morbidities like epilepsy, stroke, sub-clinical vascular brain lesions etc.[8]

There are several clinical features which have been observed in common between migraine and epilepsy like episodic attacks, presence of aura, triggering factors, and frequent familiarity. By keeping this in mind researchers have engaged in finding a common pathogenic mechanism. [9] This association may result from same environmental risk factors, direct causality and/or by a common genetic susceptibility. It has been seen that in the general population, incidence of headache is between 5 and 10%, while it is 8–23% in patients with epilepsy; in the same way, the incidence of epilepsy in the general population is 0.5–1%, but in migraine patients it can be up to 5.9%.[9] There is a new term Migralepsy, with only a few cases described in the literature because it has been observed that there is some overlap of symptoms between epilepsy and migraine.[6,9] Migraine and epilepsy may independently coexist in the same individual or may be related causally, with one leading to the other. It has drawn interest, possibly due to the finding that there is reduced seizure threshold in migraineurs, which makes this sequence biologically reasonable. Lennox & Lennox in 1960 have used this term ‘‘migralepsy’’ for first time.[10]

There is no reason that epileptic seizures which are so vulnerable to intrinsic and extrinsic precipitating factors could not be receptive to cortical changes occurring due to migraine. But this is so rare that only a few case reports are published despite the fact that migraine and epilepsy are amongst the more common brain disorders. Most of the reported cases of ‘migralepsy’ are complicated cases that do not give a clear and unequivocal migraine epilepsy sequence, or they are only occipital seizures which imitate migraine with aura.’’ Even though there is a big doubt, this condition still has been included in the recent International Classification of Headache Disorder – 3 (ICHD-3) [10]

The International Headache Society proposed International Classification for Headache Disorders (ICHD-3) which states that the following diagnostic criteria should be met:

Diagnostic criteria: [11]

A. Any headache fulfilling criterion C
B. The patient presently having or has recently had an epileptic seizure
C. Evidence of cause of headache demonstrated by:
    1. Developed simultaneously with seizure or soon after onset its onset
    2. After seizure has terminated headache has resolved spontaneously
D. Not better accounted by another diagnosis in ICHD-3.

Overlap of clinical symptomatology gives us the indication of its pathophysiological overlap. Recently, researchers have been engaged to find a common mechanism of pathogenesis but the numbers of these studies are still small. No significant association in seen in people who has history of migraine without aura. Head injuries are major cause of both headaches and seizures. Headaches associated with head injuries often have seen to be migraine type. [9]

The results of a study done by Columbia University Medical Centre in New York which was published on Epilepsia, concluded for the first time that a strong family history of epilepsy increase the chance of having migraine with aura. Data for this was taken and analyzed from a genetic study named ‘‘Epilepsy Phenome/Genome Project’’. This project involved 730 patients with epilepsy and 501 families from various US clinical centres. It demonstrated that people who have family history or more epileptic relatives have a double chance of having migraine with aura when compared with those who have less family history or epileptic relatives. This gives us with the evidence that there are various genes that are responsible for simultaneous occurrence of epilepsy and migraine. [9, 12]

The migraine and epilepsy co morbidity has been explained in a study by neuronal hyper excitability, which increases the risk of both migraine and epilepsy. In migraine, as there is excess of neuronal activity which leads to Cortical Spreading Depression (CSD- a slow wave of neuronal hyper excitability which spreads at a speed of 3–5 mm/min and subsequently followed by a cortical electrical activity depression which is the pathophysiological mechanism at the base of aura) and aura. This is then followed by subsequent recruitment of the trigeminal nucleus which is responsible for central sensitization and pain. In epilepsy, this neuronal over activity causes recruitment of larger populations of neurons to fire in a rhythmic manner and that constitutes an epileptic seizure. Headaches and migraine aura both may act as a trigger for epileptic seizures. Because of this reason some antiepileptic drugs are also used in migraine prophylaxis. Decisions regarding prophylactic treatment for migraine headaches are often taken by keeping in mind, patient's comorbidities. Mostly patients with migraine do not take proper medical care or advice; instead treat the individual acute attack with some over the counter analgesics. Those who take treatment, some do well with treatment which aims at managing the individual episodes of headache, others require additional treatment to reduce the number of migraine attacks. Abortive treatment is that which is taken only at the time of acute attack, while preventive treatment is taken on a regular basis to decrease headache frequency. [9]

In patients who have epilepsy along with migraine, the antiepileptic medications are the primary consideration. Antiepileptic medications which have demonstrated efficacy in migraine prophylaxis include topiramate (TPM) and valproic acid (VPA). Anticonvulsants which have similar mechanism of action to TPM and zonisamide (ZNS), has also been seen to be effective in migraine prophylaxis. TPM is the only medication which has strong evidence of efficacy for the treatment of chronic migraine. [13]

Although the data on this is limited, some studies have proved the use of AEDs in prophylaxis of Migraine and also show the reduction in headache frequency in known cases of migraine with epilepsy.[14] The

treatment for both disorders includes drugs which reduce the CNS transmission, though the mechanism may differ in either of disease.

The co morbidity headaches in epilepsy is controversial despite the evidence, as a result continued effort is required to increase awareness in the healthcare community.[6]

As we have limited data on this, the current study has been planned to evaluate the frequency, severity, disability and pattern of migraine headache in patients with epilepsy and migraine and effects of AEDs in patients attending epilepsy or neurology clinics in a tertiary care hospital of Ludhiana.

AIMS AND OBJECTIVES

1. To study the frequency of migraine in patients with new onset epilepsy.

2. To study the effect of various AEDs on frequency, severity, pattern and disability in patients of migraine.

REVIEW OF LITERATURE

Epilepsy is characterized by unprovoked seizures that require long term or lifelong therapy. Seizures are behavioural changes that result from abnormal, paroxysmal neuronal discharges that represent a symptom of underlying brain problem. [15] Seizure is defined as a sudden and self-limited clinical event that results from abnormal and excessive firing of cortical neurons. Seizures may result from acute head trauma, alcohol withdrawal or hypocalcaemia. The International League against Epilepsy has given a definition of epilepsy according to which the various elements are-[16]

1. At least one seizure in his or her life
2. Changes in brain that will increase the chances of future seizures.
3. Associated cognitive, neurobiologic, social and psychological disturbances.

There are different types of epilepsy and choice of AEDs depends upon etiology, semiology of epilepsy and other patient related factors.

Classification of Epileptic Seizures with suggested conventional and newly developed drugs as treatment options [2]		
Seizure Type	**Conventional Anti-Seizure Drugs**	**Recently Developed Anti-Seizure Drugs**
Partial Seizures		
Focal Aware	Carbamazepine, Phenytoin, Valproate	Brivarscetam, Eslicarbazepine, Ezogabine, Gabapentin, Lacosamide, Lamotrigine, Levetiracetam, Perampenal,

Classification of Epileptic Seizures with suggested conventional and newly developed drugs as treatment options [2]		
Seizure Type	**Conventional Anti-Seizure Drugs**	**Recently Developed Anti-Seizure Drugs**
Partial Seizures		
		Rufinamide, Tiagabine, Topiramate, Zonisamide
Focal with Impaired awareness	Carbamazepine, Phenytoin, Valproate	Brivarscetam, Eslicarbazepine, Ezogabine, Gabapentin, Lacosamide, Lamotrigine, Levetiracetam, Perampenal, Rufinamide, Tiagabine, Topiramate, Zonisamide
Focal to bilateral tonic-clonic	Carbamazepine, Phenobarbital, Phenytoin, Primidone, Valproate	Brivarscetam, Eslicarbazepine, Ezogabine, Gabapentin, Lacosamide, Lamotrigine, Levetiracetam, Perampenal, Rufinamide,

Classification of Epileptic Seizures with suggested conventional and newly developed drugs as treatment options [2]		
Seizure Type	**Conventional Anti-Seizure Drugs**	**Recently Developed Anti-Seizure Drugs**
Partial Seizures		
		Tiagabine, Topiramate, Zonisamide
Generalized Seizures		
Absence seizure	Ethosuximide, Valproate, Clonazepam	Lamotrigine
Myoclonic seizure	Valproate, Clonazepam	Levetiracetam
Tonic-clonic seizure	Carbamazepine, Phenobarbital, Phenytoin, Primidone, Valproate	Lamotrigine, Levetiracetam, Topiramate

Anti epileptic drugs

The first antiepileptic drug to be discovered was bromide, followed by Phenobarbital (PB) that was the first synthetic organic agent found to have antiseizure activity.[17] Merritt and Putnam, who developed the electroshock seizure test in experimental animals, discovered the ability of diphenylhydantoin to suppress seizure without causing sedation.[2] The chemical structure of the drugs introduced before 1965 resembled PB and included hydantoins and succinimides. This was followed by development of iminostilbines (carbamazepines), branched chain carboxylic acid (valproic acid) and more recently phenyltriazines (lamotrigine), cyclic analogue of GABA (gabapentin), sulfamate

substituted monosacchride (topiramate), nipecotic acid derivatives (tiagabine) and pyrrolidine derivative (levetiracetam).[2]

Mechanism of action of antiepileptic drugs [18]

There are four proposed mechanisms; AEDs may have any one or more than one (in combination)

1. Inhibition of sodium currents – by conventional antiepileptics like carbamazepine, phenobarbital, phenytoin, valproate
2. Enhance GABA-ergic inhibition - by novel antiepileptic drugs like tiagabine and vigabatrin.
3. Inhibition of excitatory neurotransmitter (Glutamate)
4. Decreasing influx of calcium ions into neurons via a specific subunit of voltage-dependent calcium channels e.g eslicarbazepine, lamotrigine

Newer Antiepileptic Drugs

Compared to traditional AEDs long term administration of new AEDs elicits fewer ADRs, fewer drug interactions and teratogenicity. These characteristics increase drug compliance although the antiepileptic effects of the new AEDs are not greater than of traditional AEDs[8]

ADRs with newer AEDs vary from mild to life-threatening, and many studies have been conducted to compare AEDs on basis of their CNS, psychiatric or other general ADRs.[13] Family members are often more aware of behavioural changes than the patient. [19]

ADR differ in severity depending upon different AEDs, mostly occur during early or initial phase of the treatment. Some are related to pharmacodynamic, often affected by the dose and rate of initiation, while other concerns are peculiar to the drug. Thus, a common reason for changing medication is lack of tolerability.[20] AEDs have many ADR, and many studies have compared AEDs based on their CNS, psychiatric or general medical ADR. Various studies concluded that CNS-related ADR as the main ADR in oxcarbazepine (OXC), zonisamide (ZNS) and topiramate (TPM) consumption.[14]

Behavioural side effects can occur with levetiracetam (LEV), as well as with TPM, ZNS and PB. Irritability and hostility are the main concerns with LEV, often seen soon after initiation. It was reported in a study of 629 patients who were given LEV to compare its effects on older versus younger adults: 31.7% of younger and 40.7% of older patients reported intolerability to LEV on at least one occasion. In both age groups, psychiatric and behavioural side effect were the most common ADR associated with LEV.[20]

Migraine headache afflicts 10-20% of the population. Although it is a specific neurological syndrome, the manifestations vary widely. The broad types are migraine with aura, migraine without aura and several other rare types. It can be unilateral, bilateral or both. It has a widespread pathology in patients both with epilepsy and non-epileptic. However studies have shown reduction in headache frequency in known cases of migraine with epilepsy with AEDs, benefitting both epilepsy and migraine.

ICHD 3 Criteria for Migraine [11]

1. Migraine
   - 1.1 Migraine without aura
   - 1.2 Migraine with aura
     - 1.2.1 Migraine with typical aura
       - 1.2.1.1 Typical aura with headache
       - 1.2.1.2 Typical aura without headache
     - 1.2.2 Migraine with brainstem aura
     - 1.2.3 Hemiplegic migraine
       - 1.2.3.1 Familial hemiplegic migraine (FHM)
         - 1.2.3.1.1 Familial hemiplegic migraine type 1 (FHM1)
         - 1.2.3.1.2 Familial hemiplegic migraine type 2 (FHM2)
         - 1.2.3.1.3 Familial hemiplegic migraine type 3 (FHM3)
         - 1.2.3.1.4 Familial hemiplegic migraine, other loci
       - 1.2.3.2 Sporadic hemiplegic migraine (SHM)
     - 1.2.4 Retinal migraine
   - 1.3 Chronic migraine

1.4 Complications of migraine

1.4.1 Status migrainosus

1.4.2 Persistent aura without infarction

1.4.3 Migrainous infarction

1.4.4 Migraine aura-triggered seizure

1.5 Probable migraine

1.5.1 Probable migraine without aura

1.5.2 Probable migraine with aura

1.6 Episodic syndromes that may be associated with migraine

1.6.1 Recurrent gastrointestinal disturbance

1.6.1.1 Cyclical vomiting syndrome

1.6.1.2 Abdominal migraine

1.6.2 Benign paroxysmal vertigo

1.6.3 Benign paroxysmal torticollis

Migraine without aura

A. At least five attacks fulfilling criteria mentioned below (B, C, and D)
B. Attack lasting for 4 to 72 hours
C. Having at least any 2 of these characteristics: aggravation by or causing avoidance of routine physical activity, pulsating quality, moderate or severe pain intensity, unilateral location.
D. Having at least one of these conditions during the headache: nausea and/or vomiting, photophobia or phonophobia

Migraine with aura

A. At least two attacks fulfilling below mentioned criteria (B and C)
B. Having 1 or more of fully reversible aura symptoms like brainstem, motor, retinal, sensory, speech and/or language, visual
C. Having at least 2 of these characteristics: at least one aura symptom spreads gradually over at least 5 minutes and/or two or more symptoms occur in succession; individual aura lasts 5 - 60

minutes; at least one symptom of aura is unilateral; the aura is accompanied or followed within 60 minutes by headache

Episodic migraine

Episodic migraine is not included in the ICHD-3, but its definition in the literature is recognized as zero to 14 headache days per month.

Chronic migraine

A. Headaches for at least 15 days each month for more than 3 months and fulfilling below mentioned criteria B and C
B. Occurring in patients with at least 5 attacks fulfilling criteria in the Migraine with Aura or Migraine without Aura sections
C. For at least eight days each month for more than 3 months, fulfil any of the below mentioned criteria:
D. Criteria C and D for Migraine without Aura section
E. Criteria B and C for Migraine with Aura section
F. Believed by the patient to be migraine at onset and relieved by triptan or ergot derivative

Medication- overuse headache

Regular intake of ergotamine, triptan, or opioid medications for a total of at least 10 days per month or nonopioid medications (e.g., NSAIDs, acetaminophen) for at least 15 days (each month).

A. Headache occurring on at least 15 days per month in a patient with a pre-existing headache disorder
B. Regular overuse for more than three months of one or more drugs that can be taken for acute and/or symptomatic treatment of headache[21]

Various treatment options for migraine prophylaxis are:- [22]

- Angiotensin II blockers-Candesartan
- Anti-convulsants
  - Sodium valproate
  - **Topiramate**

- **Gabapentin**

- Anti-serotonergic (Anti 5-HT) drugs
  - Pizotifen
  - Methysergide
- Beta-blockers
  - Propranolol
  - Metoprolol
  - Atenolol
  - Nadolol
  - Timolol
- CGRP pathway monoclonal antibodies
- Calcium channel blockers
  - Flunarizine
- Non-steroidal anti-inflammatory drug (NSAIDs)
  - Naproxen
- Tricyclic antidepressants (TCAs)
  - Amitriptyline
  - Dosulepin
  - Nortriptyline

For acute attack, various drugs can be categorised as: - [22]

- Nonspecific Abortive Migraine Therapy
  - NSAIDs –Aspirin, Ibuprofen
- Migraine specific medications
  - Triptans – Sumatriptan, Rizatriptan
  - Ergotamine derivatives-Ergotamine, Dihydroergotamne

Epilepsy and Migraine are chronic central nervous system disorders that mainly manifest with episodic or recurrent neurological dysfunction which returns to symptom-free baseline status between attacks [23] Both epilepsy and migraine share many risk factors and pathophysiological mechanisms[24,25,26]

As they share the pathophysiological mechanism, several AEDs are being prescribed for migraine prevention.[27,28,29] Among them, TPM and VPA are highly effective in migraine prophylaxis; while lamotrigine (LTG) efficacy is still not clear [26]

Jackson et al has done a meta-analysis which reported equal effect of LTG and TPM in migraine prophylaxis. TPM, LTG and VPA are among the most frequently used AEDs. However, VPA is used with caution among women because of its teratogenic effects and decreased IQ scores in children born to mothers taking VPA. All the three AEDs have specific adverse events (AEs); tremor, weight gain, nausea, and hair loss are the most frequent with VPA; parenthesis, cognitive dysfunction, language disturbances and weight loss with TPM. AEs associated with AEDs have negative impact on patient's life and is a big hurdle like treating the disease and compliance of patient. Reports have shown that migraineurs have a higher prevalence of AEs with TPM use when compared to its use in patients with epilepsy alone [26].

Various clinical features have been observed in common between epilepsy and migraine such as [9]

- Both are manifested as periodic attacks and both return to normality between crisis
- Both have same precipitating factors, such as stress, sleep deprivation, exposure to bright flash light.
- Both, often, have genetic involvement or family history
- Usually preceded with a transient neurological symptoms (aura)
- Frequently associated with psychological symptoms
- Occurrence of headache before, during or after seizures
- Unleashing of a seizure with a typical migraine aura
- Experiencing mental confusion or narrowing of consciousness with migraine similar to those with seizure

The above mentioned overlap in clinical manifestations or symptomatology might indicate pathophysiological overlaps.[9]

Recent years researchers are really engaged in finding a common pathogenic mechanism but still we have small number of studies on this. From various studies on incidence of disease we understand how either

epilepsy among migraine patients or migraine among patients with epilepsy is more frequent than in the general population. According to the data, incidence of headache is between 5 and 10%, in the general population while it is 8–23% in patients with epilepsy. In the same way, the incidence of epilepsy is 0.5–1% in the general population but in migraine patients it can be up to 5.9%.[26]

Migraine and epilepsy can be associated due to:

- Common genetic susceptibility
- Direct causality
- Similar environmental risk factors

The most common, direct cause is represented by ischemic strokes. It is seen that migraine can lead to silent or clinically considerable strokes. This clearly explains the increased risk of developing epilepsy in people with the history of migraine.[15]

Various epidemiological studies have also revealed that both the diseases are co morbid in many individuals. Both are now acknowledged as originating from electrical disturbances in the brain, although there is involvement of multiple pathogenic mechanisms as they have wider manifestations. In migraine there is an initial increase of neuronal activity which leads to cortical spreading depression and aura, and there is subsequent recruitment of the trigeminal nucleus which leads to central sensitization and pain.[9] In epilepsy, neuronal over activity recruit larger population of neurons which fire in a rhythmic manner and constitute an epileptic seizure. Headaches and migraine aura may act as a trigger for epileptic seizures. Epilepsy is frequently accompanied by preictal, ictal, and postictal headaches which often have features of migraine. Genetic links are also evident between the two disorders, and are particularly manifest in the familial hemiplegic migraine syndromes where many different mutations can produce either migraine, epilepsy, or both. [30]

Also, there are various medications which are found to be effective for both migraine and epilepsy, which again points to a commonality and overlap between the two disorders.[30]

On the whole, migraine is a functional and not a structural brain disease. In the first half of the 20th century, Harold Wolff and his colleagues largely worked on migraine which was thought to be a vascular disorder. Their experiments proposed that the aura in migraine is caused by vasospasm and ischemia in the brain, and the headache which follows is caused by vasodilatation. They conducted various studies demonstrating that vasodilation is associated with migrainous headache, and vasoconstriction may relieve it.[31] Recently in march 2015, a combination of functional magnetic resonance imaging (fMRI) imaging and electrophysiology studies concluded that migraine is an altered brain state and that there is a change in many neurochemical mediators which are responsible for excitation, inhibition, and pain.[32]

Clinical studies on role of Antiepileptic drugs in Migraine

Headache is under-recognized in patients with epilepsy and as a result, it is often under-treated. Around 7%-57% of patient with epilepsy (PWE) are reported to have active interictal headaches, among them migraine is seen in 2%-26.3% of population. [8]

A Prospective, double-blind, placebo-controlled clinical trial of Divalproex and Gabapentin for migraine prevention was done in 2001. The important efficacy variable was a decrease in the 28-day frequency of migraine headache. It was seen that the subjects who received divalproex at doses up to 1500mg/day for 12 weeks achieved significant decreases in the migraine frequency. This was also observed with gabapentin.[33]

Placebo-controlled, double-blind parallel group study done on 69 patients, they were randomized to LEV 1000 mg/day, TPM 100 mg/day, or placebo, showed that patients were likely to experience more than 50% reduction in headache frequency with LEV when compared with placebo. Even though it was small but difference was significant which favours the efficacy of TPM. [5] Similarly, another study of 85 patients randomized to LEV 500 mg/day, VPA 500 mg/day, or placebo, showed 50% decrease in headache frequency in the LEV group compared with the placebo, with no statistical difference in improvement between LEV

and VPA. Small-scale trials and conflicting evidence showed the need for large-scale studies to establish evidence for LEV's use in migraine prevention.[5]

There is conflicting evidence regarding the use of oral LEV for migraine prevention. A 2011 placebo-controlled, crossover trial found 3000 mg of LEV had not produced a significant reduction in migraine frequency. However, researchers did show a trend toward decreased headache severity, disability and frequency with LEV. Whereas a prospective randomized placebo-controlled study of 52 patients showed LEV at lower dose resulted in a lower headache rate as compared with placebo.[5]

Recently US FDA approved TPM for migraine prophylaxis. It is a neuromodulator which has a unique structure that provides multiple mechanisms of action and can influence the activity of voltage-activated Na^{+} channels, Ca^{++} channels, AMPA/kainate subtype of glutamate receptors and the GABA - A receptor.[13,34,35]

Among all the antiepileptic drugs, the best data for effectiveness in the prevention of migraine is available for VPA and TPM only.[13,34,35]

Recently in 2019 a study was conducted in Nagpur on 60 patients to compare the efficacy and safety of low-dose sodium valproate 500 mg once daily and low-dose propranolol 40 mg once daily sustained release in the prophylaxis of common migraine headache. The main finding of this study indicates that both low-dose sustained release formulation of propranolol and low-dose sodium valproate significantly decreased the frequency, severity, and duration of headache. Maximum decrease in all the parameters (frequency, severity, and duration) of migraine headache in both the groups was observed on second visit i.e. at 4 weeks, thus indicating that both have a similar onset of action and rate of symptomatic improvement. On subsequent visit, there was a further gradual decrease in the frequency, severity, and duration of headache, indicating that there was sustained improvement throughout the study without loss of efficacy.[36]

Mode of action of various AEDs

Valproate has broad-spectrum antiepileptic efficacy, is also effective in migraine prophylaxis. The mechanism by which it acts in migraine prophylaxis is not fully clear although there is involvement of indirect increase in GABA.[36]

It act by blocking-sustained repetitive firing through Na^+ channels, inhibit the GABA mediated neuronal firing and enhances GABA levels in the brain, inhibit action of glutamate at NMDA receptor, and modulating dopamenergic as well as serotonergic transmission[2]

Topiramate is structurally different from all other antiepileptic drugs, it blocks voltage-gated Na^+ channels and limits sustained repetitive neuronal firing same as carbamazepine and phenytoin. In addition, it enhances the action of GABA on Cl^- channels, antagonist at AMPA-type glutamate receptor, is a weak carbonic anhydrase inhibitor, and decrease the opening of L-type calcium channels [2]

Levetiracetam and Brivaracetam

Synaptic vesicle protein SV_2A mediates the anticonvulsant effects of levetiracetam. SV_2A is a transmembrane integral glycoprotein, its neuronal function is not fully understood, but binding of LEV to SV_2A affect neuronal excitability by modifying the release of glutamate and GABA. Also inhibits Ca^{2+} channels (N-type) and release Ca^{2+} from intracellular stores.[2]

Brivaracetam also binds with high affinity to SV2A and inhibits neuronal voltage-gated Na^+ channels.[2]

Lamotrigine acts in some ways similar to that of phenytoin and carbamazepine, blocks rapid neuronal firing mediated by voltage-gated Na^+ channels.[2]

Carbamazepine and Oxcarbamazepine

Like phenytoin, action is mediated by slowing of the rate of recovery of voltage-activated Na+ channels from inactivation. Its metabolite 10,11-

epoxycarbamazepine also limits sustained repetitive firing, this suggests that this metabolite can contribute to the antiseizure efficacy of carbamazepine.[2]

Oxcarbazepine is similar to carbamazepine in terms of mechanism of action. It is less-potent enzyme inducer compared to carbamazepine.

Lacosamide

It was the first antiseizure drug which prolongs the slow inactivation of voltage-gated Na+ channels and to limit sustained repetitive firing, the neuronal firing pattern characteristic of focal seizures. It also binds to collapsin response mediator protein-2 (CRMP-2), involved in neuronal differentiation and axon outgrowth, but the contribution of CRMP-2 to its antiseizure efficacy is unclear.[2]

Phenytoin

Act by slowing of the rate of recovery of voltage-activated Na+ channels from inactivation, an action that is both voltage and use dependent. At therapeutic concentrations, the effects on Na+ channels are selective. At 5- to 10-fold higher concentration, it has multiple effects, including reduction of spontaneous activity and enhancement of responses to GABA.[2]

Lamotrigine

Its action is similar to CBZ and PHT i.e. delays the recovery from inactivation of Na^+ channels. This explains its actions on focal and secondarily generalized seizures. It also inhibits release of glutamate by acting at Na^+ channels. [2]

Zonisamide

It has a unique combination of pharmacologic actions: It blocks voltage-dependent sodium and T-type calcium channels; inhibits excessive nitric oxide (NO) production, scavenging hydroxyl and NO radicals; reduces glutamate-mediated excitatory neurotransmission; and inhibits carbonic

anhydrase. All of these mechanisms in combination play a role in headache and pain modulation, mainly via neuronal stabilization. [13,34,35]

The association of migraine as common co morbidity in epilepsy is controversial despite there being a reported reduction of attacks of migraine with AEDs. As a result, we need to put continuous affords to increase awareness in the healthcare community. [8]

We have limited data on this, so we have planned a study to evaluate the frequency, severity, disability and pattern of migraine headache in patients with epilepsy and migraine and effects of AEDs.

MATERIALS AND METHODS

This follow up observational study was conducted in patients suffering from epilepsy and migraine who were on AEDs monotherapy on stable dose (3 months) attending outpatient department of epilepsy and neurology clinic of Dayanand Medical College and Hospital, Ludhiana. The study was conducted after taking prior approval from Institutional Ethics Committee.

Patients with new onset epilepsy and migraine who fulfilled the following inclusion and none of the exclusion criteria were included in the study.

INCLUSION CRITERIA

1. Age- 18 to 65 years
2. Gender- either
3. Semiology- any
4. Patient on Monotherapy (Any AED) on a stable dose for 3 months.

EXCLUSION CRITERIA

1. Non consenting individual
2. Patients on stable AED dose <3 months
3. Patients on polytherapy
4. Known case of epilepsy

Patients who fulfilled the following diagnostic criteria were considered as having Migraine headache:-

Diagnostic Criteria for Migraine [36]

Repeated attacks of headache lasting 4–72 h in patients with a normal physical examination, no other reasonable cause for the headache, and:

At least 2 of the following features:

1. Unilateral pain
2. Throbbing pain
3. Aggravation by movement
4. Moderate or severe intensity

Plus at least 1 of the following features:

1. Nausea/vomiting
2. Photophobia and Phonophobia

The patients were evaluated completely regarding the migraine attack and its association with the AEDs. Relationship of AEDs and migraine was assessed by taking a complete history about the concomitant epilepsy and migraine medications being used. All the data (including patients demographics, socioeconomic status using Modified Kuppuswamy scale)[37] was recorded on the pre structured performa. Assessment of severity of pain was done by using Global Assessment of migraine Severity (GAMS)[38] and Visual Analogue Scale (VAS).[39,40]

STUDY DESIGN

This was a follow-up observational study in which the newly diagnosed patients of epilepsy with migraine were enrolled. They were started on the monotherapy with antiepileptic drug (as per choice of treating neurologist). Assessment was done over 3 months after stable dose of AED reached. Patient demographics along with clinical characteristics such as seizures semiology, type of migraine (severity, disability, frequency and pattern) along with the complete details of the AED being used by the patient were recorded. Along with this, patients were asked to maintain a migraine diary[41] which was collected back at each subsequent visit. Need for the rescue medication – NSAIDs, Triptans or ergot derivatives (dose, frequency) was asked and recorded. Follow up was done for 3 months on monthly basis. They were interviewed for information regarding migraine history and questionnaire was filled based on that at the start of treatment.

Global assessment of migraine severity (GAMS) scale.[38]

For assessing the severity of the pain, **Global assessment of migraine severity (GAMS) scale** was used. In this the severity of the pain was obtained by asking the patient to respond to a single question: “Taking into account all aspects of your disease, how severe is your disease?” And the answer had seven response categories

(1) Not at all severe

(2) A little severe

(3) Somewhat severe

(4) Moderately severe

(5) Quite severe

(6) Very severe

(7) Extremely severe

This single severity question measured the overall severity since migraine onset. This format of GAMS and the choice of response were based on the previously validated Global Assessment of Severity in Epilepsy (GASE) which is being widely used to measure the severity in epilepsy

Visual Analogue scale (VAS) [39,40]

Another scale which was used for assessment of pain is **Visual Analogue scale (VAS)**. In this we measured the two aspects-

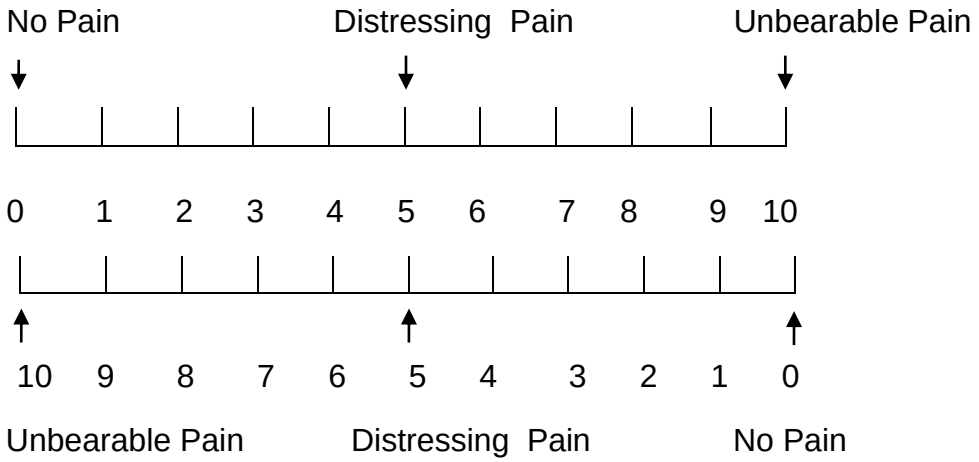
1. The intensity of the headache i.e. How strong the pain feels?
2. The unpleasantness associated with the headache i.e. How disturbing the pain is?

VAS is easy to understand and administer to the patients. It is valid method for measuring the above two aspects. This scale has the horizontal line which is anchored by the statement that represents the extremes of the aspects we want to measure. For example on one extreme of the vertical line there is “No Pain at all” and on the other extreme there will be “Unbearable Pain”, the subject was asked to place the line across the scale at the point which represent the intensity of the pain at that given time. This helped us to measure the intensity of the pain patient was feeling at that particular moment.

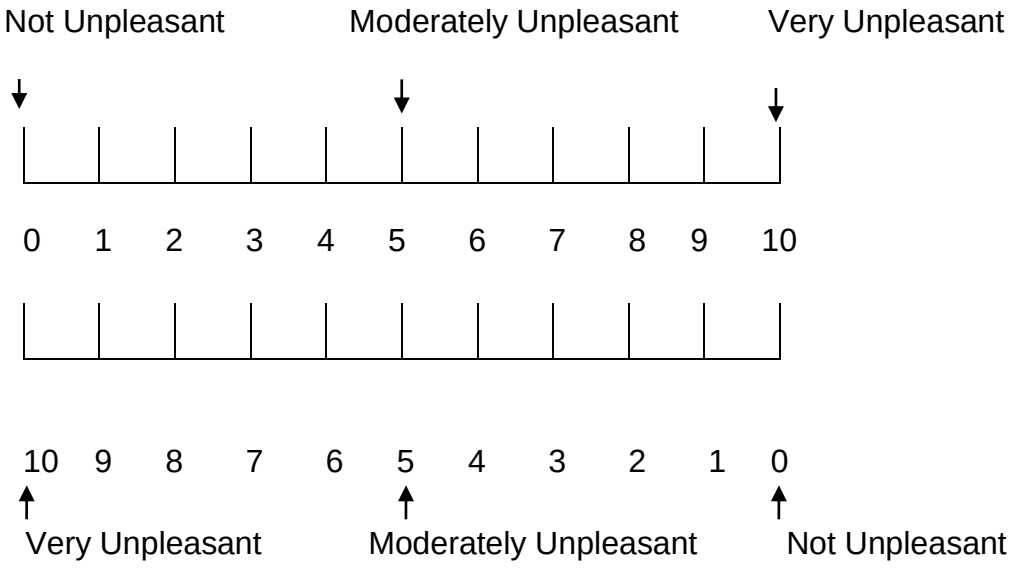
In the same way patient was asked to place a line across another VAS for the unpleasantness of the headache.

Visual Analogue Scale-

Choose a number from 0 to 10 that best describe your pain



Choose a number from 10 to 0 that best describe the unpleasantness of the headache


Not Unpleasant
Moderately Unpleasant
Very Unpleasant
0 1 2 3 4 5 6 7 8 9 10
10 9 8 7 6 5 4 3 2 1 0
Very Unpleasant
Moderately Unpleasant
Not Unpleasant

DURATION OF STUDY

Enrolment- 1 Year

Follow up- 3 Months

OUTCOME PARAMETERS

1. Assessment of improvement or worsening of migraine in terms of frequency, pattern, severity and disability in patient on AEDs.

2. Any change in pattern of migraine and need for acute treatment (rescue).

STATISTICAL ANALYSIS

The data so obtained was entered in Microsoft Excel and analyzed using descriptive statistics. It is described in terms of range; mean ± standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate.

All statistical calculations was done using SPSS (Statistical Package for the Social Science) SPSS 21 version statistical program for Microsoft Windows.

OBSERVATION AND RESULTS

This was an observational study conducted over the period of 1 year in the outpatient department of neurology and epilepsy clinic, Dayanand Medical College and Hospital, Ludhiana. The study was conducted after the prior approval from the Institutional Ethics Committee.

A total of 102 clinically diagnosed cases of new onset epilepsy (any seizure semiology) and migraine (any type) were enrolled for the study. They were started on monotherapy with AEDs and after 3 months of stable dose, follow up was done for 1st, 2nd and 3rd month after dose stabilization. Patients' demographics, including age, gender, height, weight, socioeconomic status along with detailed past and family history regarding epilepsy and migraine were recorded. Data was entered in a pre-structured performa. Study participants were categorized on the basis of seizure semiology and AEDs prescribed (according to the dose).

Migraine frequency and severity were recorded at the start of treatment and at the end of 1st, 2nd and 3rd month of follow up after 3 months dose stabilization. Severity of migraine attacks was assessed by using VAS and GAMS scale. Patients were given migraine dairy to record the migraine attacks which was collected at the end of each follow up.

Among all, 41 (40.19%) patients belonged to age group 21-30 years (Figure 1). From all the enrolled subjects, 49(48%) were from lower middle class (Figure 2). Among all, 58 (56.9%) were male and 44 (43.1%) females (Figure 3). 42(41.2%) subjects were from rural background and 60(58.8%) were from urban background (Figure 4).

When categorized on the basis of seizure semiology, 51(50%) patients were with Generalized tonic clonic seizures (GTCS), 16 (15.6%) with Complex partial seizures(CPS), 13 (12.7%) with Focal Motor, 9(8.8%) with Focal with secondary generalization, 8 (7.8%) Simple Partial Seizure (SPS), and 5 (4.9%) with Myoclonic seizures. (Figure 5)

46 (45.1%) patients had migraine with aura and in 56 (54.9%) patients it was migraine without aura. (Figure 6)

There were a number of triggering factors for migraine; some of the patients having more than one. Most common among them was stress (46.1%); exposure to sunlight (37.3%); travelling (25.5%); loud sound (17.6%); exposure to cold (9.8%); physical activity (8.8%); lack of sleep (8.8%); skipping meals (7.8%); seizure (5.9%); excessive use of mobile phones (3.9%). In 4% there was no triggering factor (Figure 7).

A questionnaire was filled by all hundred and two patients at the start of the therapy; result of questionnaire showed that 100% of the patients had facial or head pain at the start of the treatment. On an average in the last 3 month from the start of the treatment they had mean headache of 11.2 ±14.9 per month. In 38.2% of patients headache occurs more than once per day and in them mean headache attacks per day was 1.8 ± 1.9. Each attack lasted for 3.9 ± 6.7 hours. In 55.9% of patient headache was unilateral. And among them in 84.3% the pain was always on the same side. In 33% of the patient pain was located in temple, in 23.6% whole head, 21.5% it was located on the side of head, in 16.6% it was at the back of head and in 5.9% of patient it was located around the eye.(Figure 8) Majority of the patients (53.9%) were having throbbing/pulsating kind of pain followed pressing/lightening kind of pain. (Figure 9) Mean intensity of the pain (according to VAS) was 6.5 ± 2.3.

39.2% of patients experience nausea along with headache, 37.3% was sensitive to light, 35.2% sensitive to sound. 18.6% patient had forehead and facial sweating along with headache. 12.7% patients experience agitation along with headache. 5.8% patients experienced eye redness and drooping. (Figure 10) 75.6% patients had disability along with headache. 32 patients experience reversible neurological symptoms before the onset of headache, among 32, majority (93.4%) had visual symptoms and 6.6% had speech disturbance. (Figure 11)

11 patients complained of having an attack on lying flat and 4 patients complained that they had headache on coughing. (Figure 12) On asking about the treatment taking for the acute attack, it was seen that majority of the patients were taking Paracetamol 500mg (66.6%) followed by Diclofenac (18.6%), Paracetamol 650mg(15.6%), Aspirin (11.7%),Naproxen (2.9%) and Naproxen + Domperidone (1.9%).(Figure 13) None of them were taking prophylactic treatment.

When categorized on the basis of seizure semiology, there were a total 51 patients with GTCS, 42 among them were on AED alone and 9 were prescribed prophylactic treatment for migraine along with the AED.

Table 1 shows distribution of patients based on AED alone and dose in patients with migraine and GTCS.

Figure 14 shows the decrease in mean frequency with different AEDs at enrollment and at the end of 1st, 2nd and 3rd month follow up after dose stabilization in patients with GTCS.

Table 2 shows mean frequency of migraine attacks per month of 18 patients who were on VPA 20-25mg/kg.

On analysing the effect of VPA 20-25mg/kg on mean frequency of migraine, it was seen that the difference in mean frequency at the time of enrollment and 2nd month of follow up after dose stabilization was 5.50 ± 1.75 which was statistically significant (P=0.006). Difference in mean frequency at the time of enrollment and 3rd month follow up after dose stabilization is 6.33 ± 1.80 which was statistically significant (P=0.003). (Table 2)

Similarly the difference in mean frequency between 1st and 2nd month of follow up after dose stabilization was 1.83 ± 0.44 which was highly significant (P=0.001) and between 1st and 3rd month of follow up after dose stabilization was 2.67 ± 0.83 which was also statistically significant (P=0.005) (Table 2)

Table 3 shows mean frequency of migraine attacks per month of 15 patients who were taking LEV 15-20mg/kg.

On analysing the effect of LEV 15-20mg/kg on mean frequency of migraine, it was seen that the difference in mean frequency at the time of enrollment and 2nd month of follow up after dose stabilization was 5.43 ± 1.83 which was statistically significant (P=0.010). And difference in mean frequency at the time of enrollment and 3rd month after dose stabilization is 6.40 ± 1.99 which was statistically significant (P=0.006). (Table 3)

Similarly the difference in mean frequency between 1st and 2nd month of follow up after dose stabilization was 1.83 ± 0.45 which was highly significant (P=0.001) and between 1st and 3rd month of follow up after dose stabilization was 2.8 ± 0.67 which was also highly significant (P=0.005).The difference in mean frequency between 2nd and 3rd month of follow up after dose stabilization was 0.96 ± 0.42 which was statistically significant (P=0.038). (Table 3)

Three patients on CBZ 20mg/kg, showed decrease in mean frequency at the end of 3rd month follow up after dose stabilization from 13.5 ± 8.26 (at enrollment) to 7.8 ± 7.52 (3rd month follow up after dose stabilization) attacks per month. Two patients on OXC 900-1200mg/day showed decrease in mean frequency at the end of 3rd month follow up after dose stabilization from 9.5 ± 11.31 (at enrollment) to 4.8 ± 6.72 (3rd month follow up after dose stabilization) attacks per month. (Figure 14)

There was only one patient on LAC 350mg/day, BRV 100mg/kg and PHT 400mg/day each. With LAC 350mg/day they showed decrease in mean frequency from 12 at enrollment to no headache attack at the end of 1st month and the subsequent follow ups after dose stabilization. BRV 100mg/kg they showed decrease in mean frequency from 12 at enrollment to 2 headache attacks per month at the end of 1st month and the subsequent follow ups after dose stabilization. With PHT 400mg/kg there was decrease from 5 at enrollment to 1 attack per month at the end of 3rd month follow up after dose stabilization. (Figure 14)

Figure 15 shows the decrease in mean VAS score with different AEDs at enrollment and at the end of 1st, 2nd and 3rd month follow up after dose stabilization in patients with GTCS

Table 4 shows mean VAS score of 18 patients who were on VPA 20-25mg/kg

Effect of VPA 20-25mg/kg on mean VAS score of migraine was also analysed, it was seen that the difference in mean VAS score at enrollment and 2nd month of follow up after dose stabilization was 1.27 ± 0.58 which was statistically significant (P=0.044) and difference in mean VAS score at enrollment and 3rd month follow up after dose stabilization is 3.05 ± 0.75 which was statistically significant (P=0.001). Similarly the difference in mean VAS score between 1st and 3rd month of follow up after dose stabilization was 2.11 ± 0.66 which was also statistically significant (P=0.006) (Table 4)

Table 5 shows mean VAS score of 15 patients who were on LEV 15-20mg/kg.

With LEV 15-20mg/kg, it was seen that difference in mean VAS score at enrollment and 2nd month of follow up after dose stabilization was 2.6 ± 0.76 which was statistically significant (P=0.004) and difference in mean VAS score at enrollment and 3rd month follow up after dose stabilization is 4.53 ± 0.76 which was highly significant (P=0.0001). Similarly the difference in mean VAS score between 1st and 2nd month of follow up after dose stabilization was 1.5 ± 0.63 which was significant (P=0.029) and between 1st and 3rd month of follow up after dose stabilization was 3.46 ± 0.79 which was also statistically significant (P=0.001) (Table 5)

At the end to 3rd month follow up after dose stabilization mean VAS score was reduced from 8.3 ± 1.53 (at enrollment) to 5 ± 4.36 with CBZ 20mg/kg and 5 ± 0.00 to 2 ± 2.83 with OXC 900-1000mg/day. With LAC 350mg/day and BRV 100mg/kg it reduced from 9 (at enrollment) to 0 and 9 (at enrollment) to 7 respectively at the end of 1st month and subsequent

follow ups after dose stabilization. LEV 8mg/kg and PHT 400mg/day showed no decrease in severity (Figure 15)

Figure 16 shows the decrease in mean GAMS with different AEDs at enrollment and at the end of 1st, 2nd and 3rd month follow up after dose stabilization in patients with GTCS

Table 6 shows mean GAMS score of 18 patients who were on VPA 20-25mg/kg

With GAMS, another scale which was used for assessing the severity of migraine, it was seen that with VPA 20-25mg/kg the difference in mean GAMS score at enrollment and 2nd month of follow up after dose stabilization was 0.78 ± 0.04 which was statistically significant (P=0.044) and difference in mean GAMS score at enrollment and 3rd month follow up after dose stabilization was 1.83 ± 0.45 which was also statistically significant (P=0.001). (Table 6)

Similarly the difference in mean GAMS score between 1st and 3rd month of follow up after the dose stabilization was 1.16 ± 0.41 which was statistically significant (P=0.01). The difference in mean GAMS score between 2nd and 3rd month of follow up after dose stabilization was 1.05 ± 0.36 which was also statistically significant (P=0.008). (Table 6)

Table 7 show mean GAMS score of 15 patients who were on LEV 15-20mg/kg.

With LEV 15-20mg/kg, mean difference in GAMS score at enrollment and 2nd month of follow up after dose stabilization was 0.93 ± 0.48 which was statistically significant (P=0.001) and difference in mean GAMS score at enrollment and 3rd month follow up after dose stabilization was 2.86 ± 0.45 which was highly significant (P=0.0001). (Table 7)

Similarly the difference in mean GAMS score between 1st and 3rd month of follow up after dose stabilization was 2.07 ± 0.46 which was statistically significant (P=0.001). The difference in mean GAMS score

between 2nd and 3rd month of follow up after dose stabilization was 0.93 ± 0.37 which was statistically significant (P=0.02). (Table 7)

Mean GAMS score reduced from 4.7 ± 2.08 to 2.3 ± 2.08 with CBZ 20mg/kg and 1.5 ± 0.71 to 1 ± 1.41 with OXC 900-1000mg/kg at the end of 3rd month follow up after dose stabilization. With LAC 350mg/day and BRV 100mg/kg GAMS score reduced from 7 at enrollment to 0 and 5 at enrollment to 4 respectively at the end of 1st and subsequent months follow up after dose stabilization. LEV 8mg/kg and PHT 400mg/day showed no decrease in severity (Figure 16)

Table 8 shows distribution of patients based on AED + Propranolol and dose in patients with migraine and GTCS.

Patients who were on VPA 20-25mg/kg + Propranolol 10mg/day showed decrease in mean frequency at the end of 3rd month follow up after dose stabilization from 15.5 ± 11.23 (at enrollment) to 2.5 ± 1.15 per month. With LEV 15-20mg/kg + Propranolol 10mg/day, decrease in mean frequency at the end of 3rd month follow up after dose stabilization from 13.5 ± 14.8 (at enrollment) to 6.5 ± 9.6 per month. With PHT 400mg/kg + Propranolol 10mg/day decrease in mean frequency of headache at the end of 3rd month follow up after dose stabilization from 30 (at enrollment) to 7 attacks per month. With LAC 350mg/day + Propranolol 10mg/day decrease in mean frequency at the end of 2nd and 3rd month follow up after dose stabilization from 20 (at enrollment) to 4 headache attacks per month (Figure 17)

In the same 8 patients, the VPA 20-25mg/kg + Propranolol 10mg/day showed decrease in mean VAS score at the end of 3rd month follow up after dose stabilization from 8.75 ± 0.96 (at enrollment) to 6.00 ± 2.31. With LEV 15-20mg/kg + Propranolol 10mg/day decrease in mean VAS score at the end of 3rd month follow up after dose stabilization was from 9.00 ± 1.00 (at enrollment) to 3.67 ± 3.21. With PHT 400mg/kg + Propranolol 10mg/day decrease in mean VAS score at the end of 3rd month follow up after dose stabilization from 5 (at enrollment) to 4. With LAC 350mg/day + Propranolol 10mg/day decrease in mean VAS score

at the end of 2nd and 3rd month follow up after dose stabilization from 8 (at enrollment) to 5. (Figure 18)

Similarly GAMS showed decrease from 4.75 ± 0.96 at enrollment to 3.25 ± 1.50 with VPA 20-25mg/kg + Propranolol 10mg/day at the end of 3 months follow up after dose stabilization, 4.33 ± 1.53 (at enrollment) to 2.33 ± 2.08 with LEV 20mg/kg + Propranolol 10mg/day, with PHT 400mg/kg+ Propranolol 10mg/day from 3 (at enrollment) to 2 and with LAC 350mg/day + Propranolol 10mg/day it decreased from 5 (at enrollment) to 3 decrease at the end of 2nd and 3rd month follow up after dose stabilization. (Figure 19)

There were 16 patients with Complex partial seizures, 13 were only on AEDs and 3 were on prophylactic therapy along with AED.

Table 9 shows distribution of patients based on AED alone and dose in patients with migraine and Complex partial seizures.

Maximum decrease in frequency was seen with LEV 8mg/kg i.e. from 27 at enrollment to 7 headache attacks per month at 2nd month follow up and to 2.5 by the end of 3rd month after dose stabilization. With LEV 15-20mg/kg it decreased in mean frequency from 10.12 ± 13.33 at enrollment to 3.13 ± 3.88 attacks per month at the end of 3rd month follow up after dose stabilization. With CBZ 15-20mg/kg mean frequency decreased from 11.75 ± 10.25 at enrollment to 7.50 ± 10.61 attacks per month at the end of 3rd month follow up after dose stabilization. With OXC 900 -1200 mg/day mean frequency decreased was from 7.63 ± 8.37 at enrollment to 5.7 ± 6.25 attacks per month at the end of 3rd month follow up after dose stabilization. With LAC 350mg/day frequency reduced from 1 attack per month at enrollment to no attack at the end on 1st month and the subsequent follow up after dose stabilization. And with VPA 25mg/kg there was no decrease in frequency. (Figure 20)

With LEV 15-20mg/kg VAS reduced from 6.75 ± 2.50 to 2.75 ± 3.40 and GAMS from 4.25 ± 2.06 to 4.00 ± 1.50 at the end of 3rd month follow up after dose stabilization. With LEV 8mg/kg VAS score reduced from 8 to

3 and GAMS score reduced from 4 to 2 at the end of 3rd month after dose stabilization. There is no change seen in severity with VPA 20-25mg/kg and OXC 900-1200mg/kg. With CBZ 15-20mg/kg VAS score reduced from 8 to 4 and GAMS score reduced from 4.50 to 2 at the end of 3rd month follow up after dose stabilization. (Figure 21 & 22)

Table 10 shows distribution of patients based on AED + Propranolol and dose in patients with migraine and Complex partial seizuress.

With LEV 20mg/kg + Propranolol 10mg/day mean frequency decreased from 30 (at enrollment) to 10 attacks per month by end of 3rd month follow up after dose stabilization. With LEV 8mg/kg + Propranolol 10mg/day mean frequency decreased from 15 (at enrollment) to 4.5 attacks per month by the end of 2nd and 3rd month follow up after dose stabilization. With OXC 1200mg/day + Propranolol 10mg/day mean frequency decreased from 12.5 (at enrollment) to 3.5 attacks per month by the end 1st and subsequent follow ups after dose stabilization (Figure 23)

With LEV 8mg/kg + Propranolol 10mg/day mean VAS decreased from 8 (at enrollment) to 4.5 and GAMS score decreased from 5 (at enrollment) to 2 by the end of 2nd and 3rd month follow up after dose stabilization. There was no decrease in severity with LEV 20mg/kg + Propranolol 10mg/day and OXC 1200mg/day + Propranolol 10mg/day. (Figure 24 & 25)

There were total 13 patients with focal seizure, 11 were on only AEDs and 2 were taking prophylactic treatment for migraine along with AEDs.

Table 11 shows distribution of patients based on AED alone and dose in patients with migraine and Focal seizure

Maximum decrease in mean frequency was seen with LEV 8mg/kg i.e. from 14.50 ± 18.38 at enrollment to 2.00 ± 0.71 attacks per month at end of 3rd month follow up after dose stabilization but no change was seen at the end of 1st follow up after dose stabilization. With CBZ 20mg/kg mean frequency decreased from 20 at enrollment to 10 attacks per

month at 3rd month follow up after dose stabilization. With LAC 350mg/day mean frequency decreased from 18.25 ± 16.62 attacks per month at enrollment to 7.5 ± 10.61 attacks per month at the end of 2nd month follow up and again rose to 10.00 ± 14.14 attacks per month by the end of 3rd month after dose stabilization. LEV 15-20mg/kg from 6.00 ± 7.72 at enrollment to 1.50 ± 2.12 attacks per month and least with OXC 1000-1050mg/day from 3.00 ± 2.12 at enrollment to 1.25 ± 0.35 at the end of 3rd month follow up after dose stabilization. (Figure 26)

Based on VAS and GAMS score severity was decreased to almost same extent with all the AEDs (Figure 27 & 28)

Table 12 shows distribution of patients based on AED + Propranolol and dose in patients with migraine and Focal seizure.

In both the patient's there was severe decrease in frequency. With LEV 18mg/kg + Propranolol 10mg decrease in frequency was from 12 at enrollment to 2 headache attacks per month at 2nd month follow up and it further decreased to no attack at the end on 3rd month follow up after dose stabilization.(Figure 29) There was not much decrease in severity (Figure 30 & 31)

With PHT 350mg/day + Propranolol 10mg decrease in frequency was from 9 attacks per month to no attack at the end of 2nd and 3rd month follow up after dose stabilization. (Figure 29) There was no decrease in severity of pain based on VAS and GAMS at the end of 1st month follow up. (Figure 30 & 31)

There were total 9 patients of focal with secondary generalization, among them there were 4 patients who were only on AED and other 5 were taking prophylactic treatment along with AED

All the 4 patients who were on AED alone were taking LEV 20mg/kg, mean frequency decreased from 2.50 ± 2.50 at enrollment to 1.80 ± 1.44 attacks per month at the end of 3rd month follow up after dose

stabilization. (Figure 32). No much change in severity was seen at the end of 3rd month. (Figure 33 & 34)

Table 13 shows distribution of patients based on AED + Propranolol and dose in patients with migraine and Focal with secondary generalization seizures.

With OXC 900-1050mg/kg + Propranolol 10mg/day, mean frequency decreased from 16.50 ± 19.09 at enrollment to 2.2 ± 3.18 attacks per month at the end of 3rd month follow up after dose stabilization. With LEV 20mg/kg + Propranolol 10mg/day, mean frequency decreased from 11 at enrollment to no attack per month at the end of 3rd month follow up after dose stabilization. With PHT 400mg/day + Propranolol 10mg/day, mean frequency decreased from 5 at enrollment to 1 attack per month at end of 2nd and 3rd month follow up after dose stabilization. BRV 200mg/day + Propranolol 10mg/day showed no change in frequency of migraine attack per month during the follow up after dose stabilization. (Figure 35)

On assessing the change in severity, LEV 20mg/kg + Propranolol 10mg/day and BRV 200mg/day + Propranolol 10mg/day showed no change. With OXC 900-1050mg/kg + Propranolol 10mg/day mean VAS score decreased from 8.5 ± 0.71 at enrollment to 1 ± 1.41 and mean GAMS score decreased from 6.00 ± 0.00 at enrollment to 0.5 ± 0.71 by the end of 3rd month follow up after dose stabilization With PHT 400mg/day + Propranolol 10mg/day, VAS score decreased from 6 at enrollment to 5 and GAMS score decreased from 3 at enrollment to 2 at end of 2nd and 3rd month follow up after dose stabilization (Figure 36 & 37)

Table 14 shows distribution of patients based on AED and dose in patients with migraine and SPS.

With OXC 900mg/day decrease in mean frequency from 20 at enrollment to 5 at the end of 3rd month follow up after dose stabilization. With LEV

8mg/kg decrease in mean frequency from 3.7 at enrollment to 1.7 at the end of 3rd month follow up after dose stabilization. (Figure 38)

Table 15 shows mean frequency of 5 patients who were on LEV 15-20mg/kg.

On analysing mean frequency of migraine with LEV 15-20mg/kg, it was seen difference in mean frequency at enrollment and 3rd month follow up after dose stabilization is 8.4 ± 2.7 which was statistically significant (P=0.037). Similarly the difference in mean frequency between 1st and 3rd month of follow up after dose stabilization was 2.60 ± 0.49 which was significant (P=0.006). The difference in mean frequency between 2nd and 3rd month of follow up after dose stabilization was 1.30 ± 0.20 which was statistically significant (P=0.003). (Table 15)

Figure 39 shows the decrease in mean VAS score with different AEDs at enrollment and at the end of 1st, 2nd and 3rd month follow up after dose stabilization in patients with Simple partial seizures.

Table 16 shows mean VAS score of 5 patients who were on LEV 15-20mg/kg.

On analysing the mean VAS score with LEV 15-20mg/kg, difference in mean VAS score between 1st and 3rd month of follow up after dose stabilization was 1.00 ± 0.316 which was significant (P=0.034) (Table 16)

Table 17 shows mean GAMS score of 5 patients who were on LEV 15-20mg/kg.

With LEV 15-20mg/kg, there was no significant difference in mean GAMS score at the end of any follow up after dose stabilization. (Table 17)

With LEV 8mg/kg there was only slight decrease in severity i.e. from 7.5 (at enrollment) to 7 (VAS score) and 5 (at enrollment) to 3.5 (GAMS score) at the end of 2nd and 3rd month follow up after dose stabilization. With OXC 900mg/day, no change is seen. (Figure 39 & 40)

None of the patient with simple partial seizure was taking prophylactic treatment for migraine along with AED.

There were total 5 patients with Myoclonic seizures, among them 2 patients were on monotherapy of AED and 3 were taking prophylactic treatment for migraine along with AED.

Two patients who were only on AED were taking VPA 25mg/kg. They showed decrease in mean frequency from 12.5 at enrollment to 7.5 (Figure 41) but there was no decrease in severity at the end of 3rd month follow up after dose stabilization. (Figure 42 & 43)

Table 18 shows distribution of patients based on AED + Propranolol and dose in patients with migraine and Myoclonic seizures.

With TPA 250mg/day + Propranolol 20mg, there was decrease in mean frequency from 30.00 ± 0.00 at enrollment to 8.00 ± 0.00 attacks per month at the end of 3rd month follow up after dose stabilization. With LEV 15mg/kg + Propranolol 10mg, there was decrease in frequency from 11 at enrollment to 1 attack per month at the end of 1st and 2nd follow up and no attacks per month at the end on 3rd month follow up after dose stabilization. (Figure 44)

With TPA 250mg/day + Propranolol 20mg, there was no change in VAS and GAMS at the end of 1st and 2nd month follow up after dose stabilization. VAS and GAMS decreased from 10 (at enrollment) to 5 and 6 (at enrollment) to 2 respectively by the end of 3rd month follow up after dose stabilization. There was no change in VAS and GAMS score with LEV 15mg/kg + Propranolol 10mg. (Figure 45 & 46)

Out of total 102, there were 77 patients with disability. In 38.9% (N=30) no improvement was observed and rest 61.1% (N= 47) of patients showed reduction in migraine related disability at the end of 3rd month follow up after dose stabilization. Five patients who were taking VPA 20-25mg/kg had migraine related disability at the enrollment, 3 among them showed improvement at the end of 3rd month follow up after dose stabilization. Four patients taking VPA + propranolol had migraine

related disability at the enrollment and only one improved at the end of 3rd month follow up after dose stabilization. (Figure 47)

31 patients who were on LEV 15-20mg/kg had migraine related disability, by the end of 3rd month follow up after dose stabilization 25 of them improved. Six patients taking LEV 15-20mg/kg + propranolol had migraine related disability at enrollment, 4 improved at the end of 3rd month follows up after dose stabilization. Two patients of LEV 8mg/kg had migraine related disability at the enrollment, one showed improvement and 5 patients taking LEV 8mg/kg+ propranolol had migraine related disability at the start and 2 improved at the end of 3rd month follow up after dose stabilization. (Figure 47)

Six patients taking CBZ 20mg/kg also showed migraine related disability at the enrollment, 4 improved at the end of 3rd month follow up after dose stabilization. Only 2 patients taking OXC 900-1200mg/day showed improvement at the end of 3rd month follow after dose stabilization out of 7 who showed migraine related disability at the time of enrollment. Two patients taking OXC 900-1200mg/kg + propranolol had migraine related disability at enrollment and one showed improvement at the end of 3rd month follow up after dose stabilization. (Figure 47)

There were 4 patients on LAC 350mg/day with migraine related disability at enrollment, 3 among them showed improvement at the end of 3rd month follow up after dose stabilization. Only one patients taking TPA 250mg/day + propranolol had migraine related disability at the start of treatment and showed improvement at the end at the end of 3rd month follow up after dose stabilization. (Figure 47)

One patient taking PHT 400mg/day, two patients taking PHT 400mg/day + propranolol and one taking BRV 100mg/kg had migraine related disability at the enrollment and none of them showed improvement at the end of 3rd month follow up after dose stabilization. (Figure 47)

Figure 1

Age distribution of patients

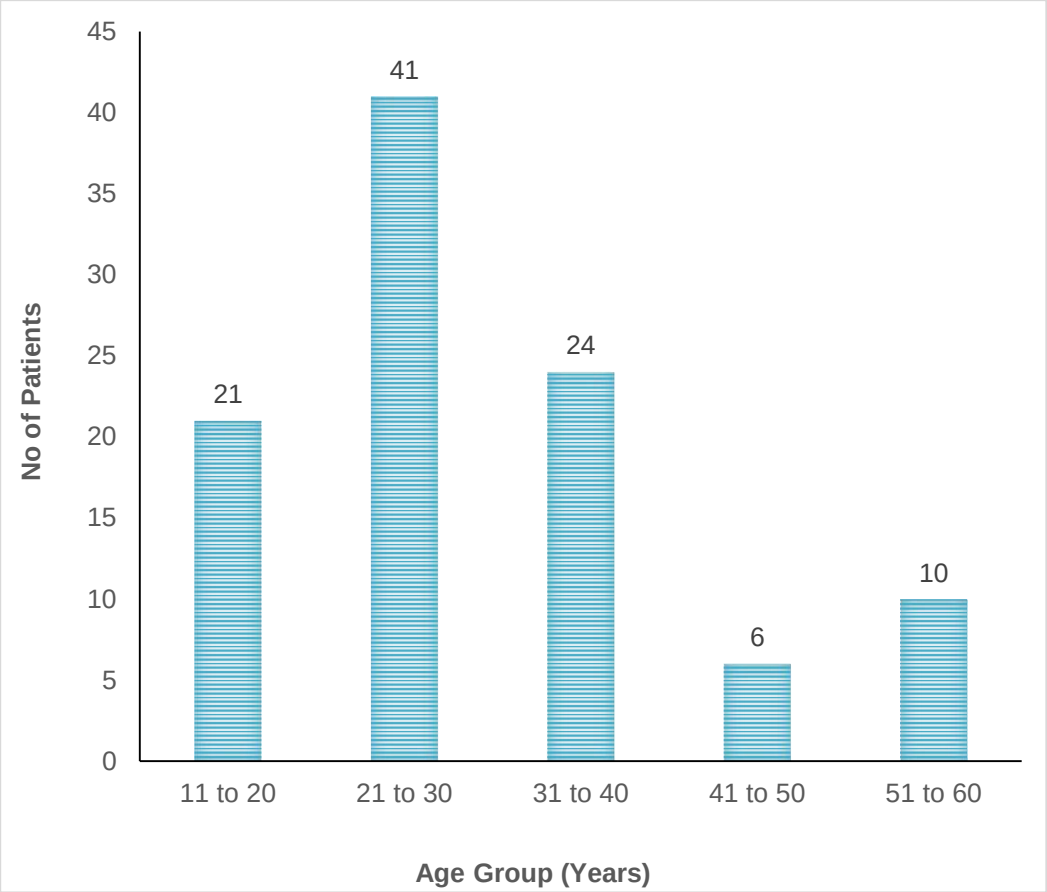


Figure 2

Socio-economic status of patients

(Modified Kuppuswamy's socioeconomic scale)

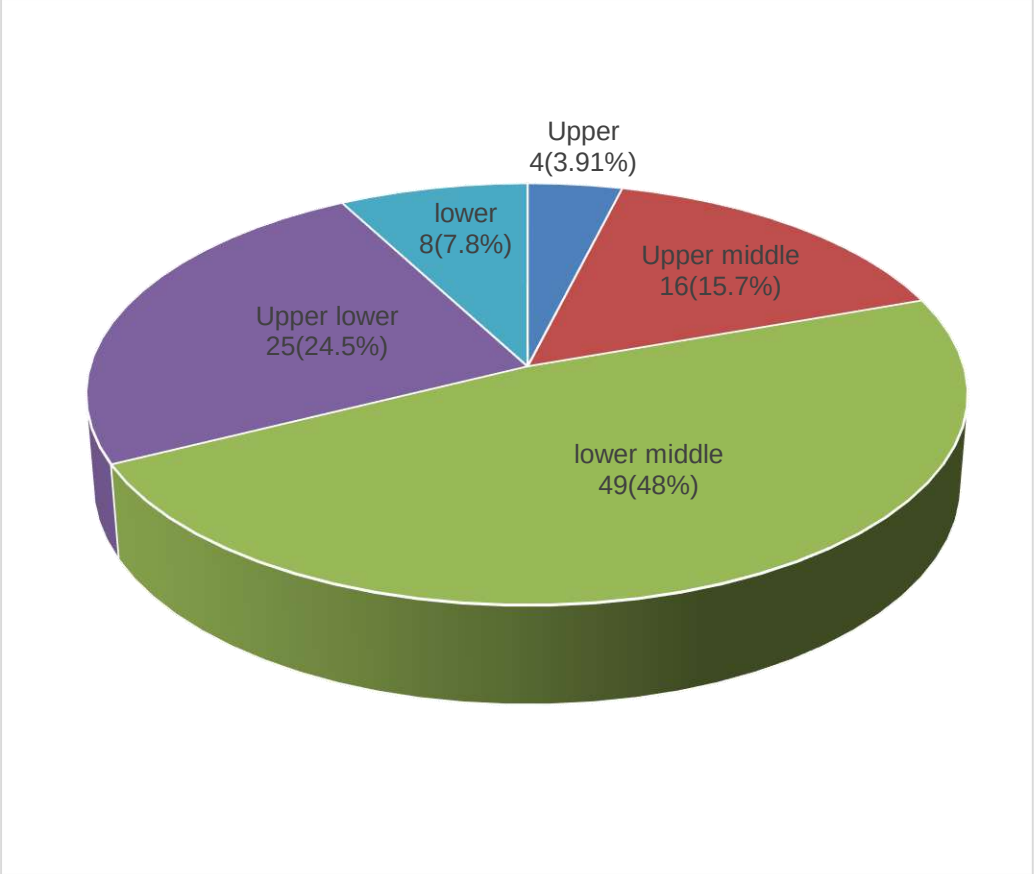


Figure 3

Gender distribution among patients

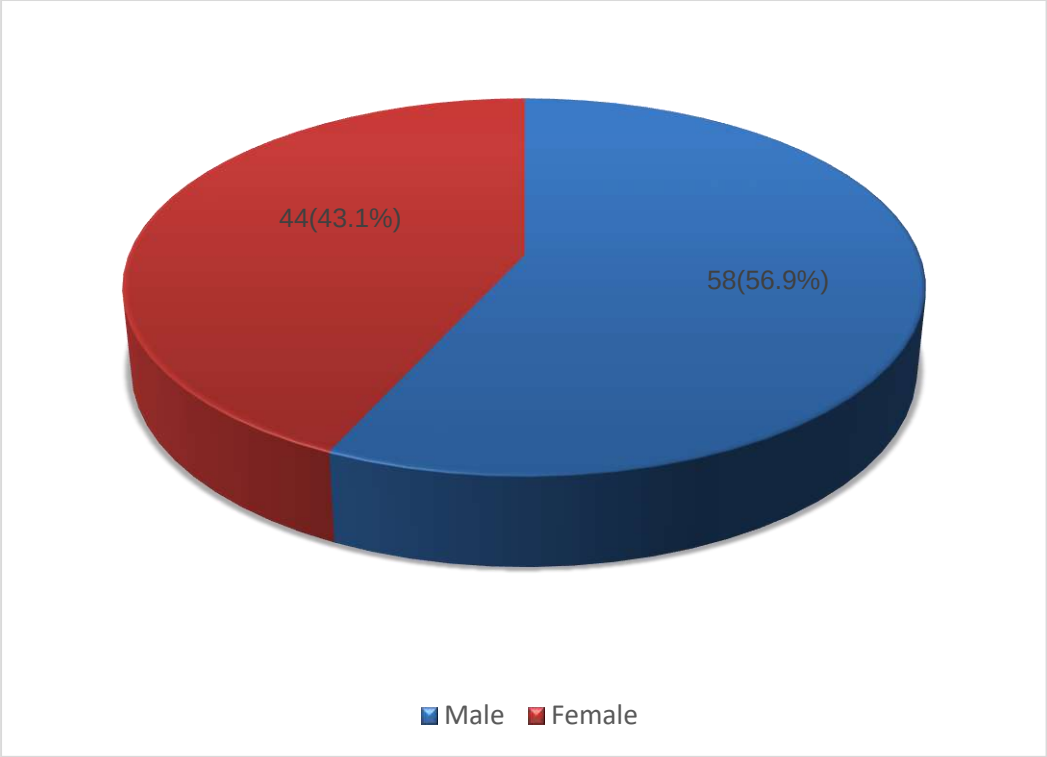


Figure 4

Residential area distribution of patients

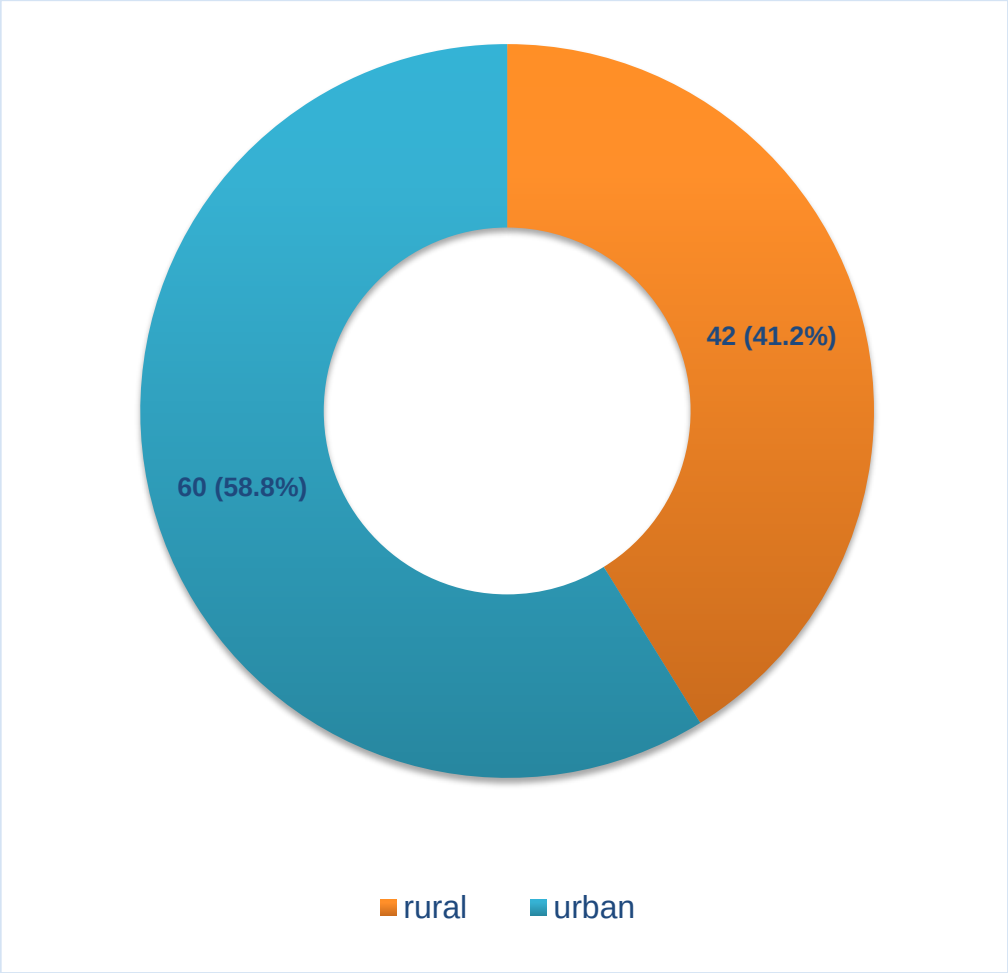


Figure 5

Seizure semiology among patients

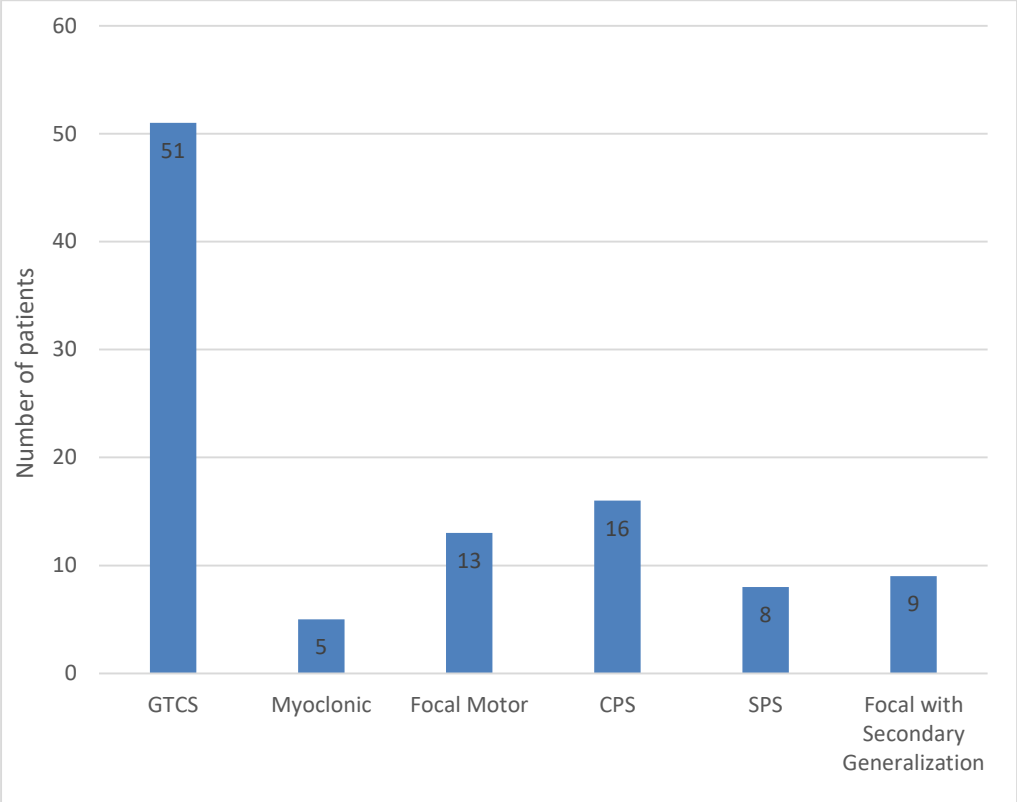


Figure 6

Distribution of patient's according to type of migraine

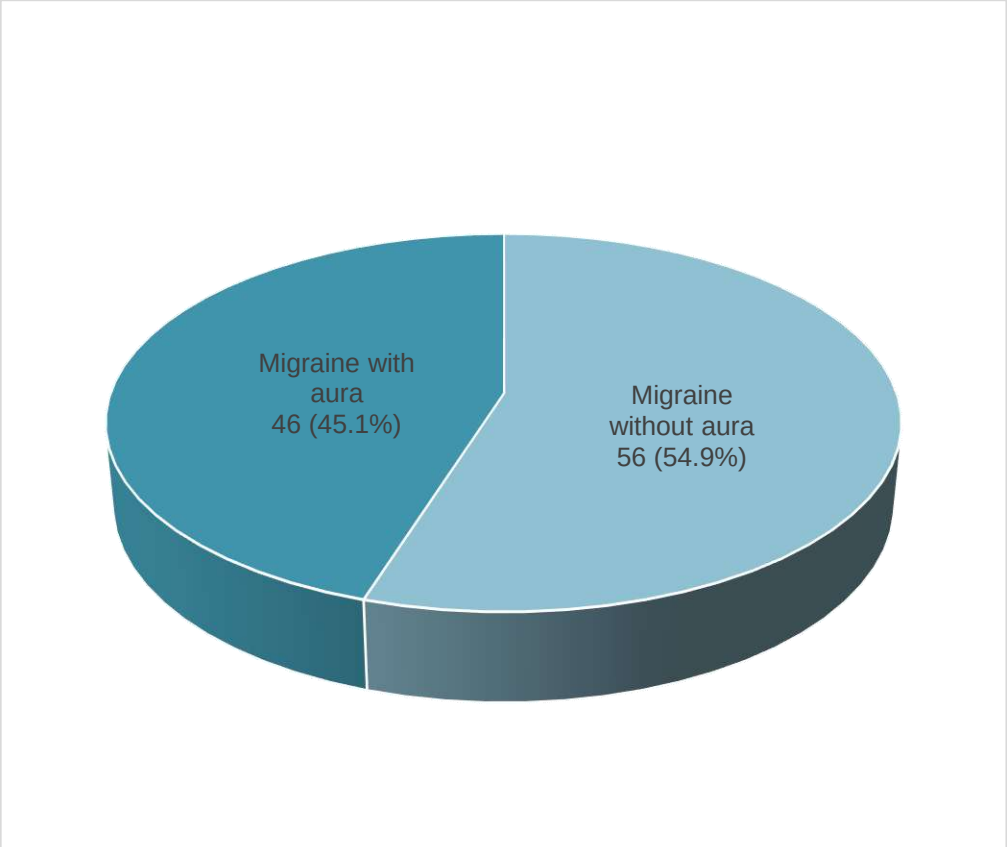


Figure 7

Triggering factors for migraine

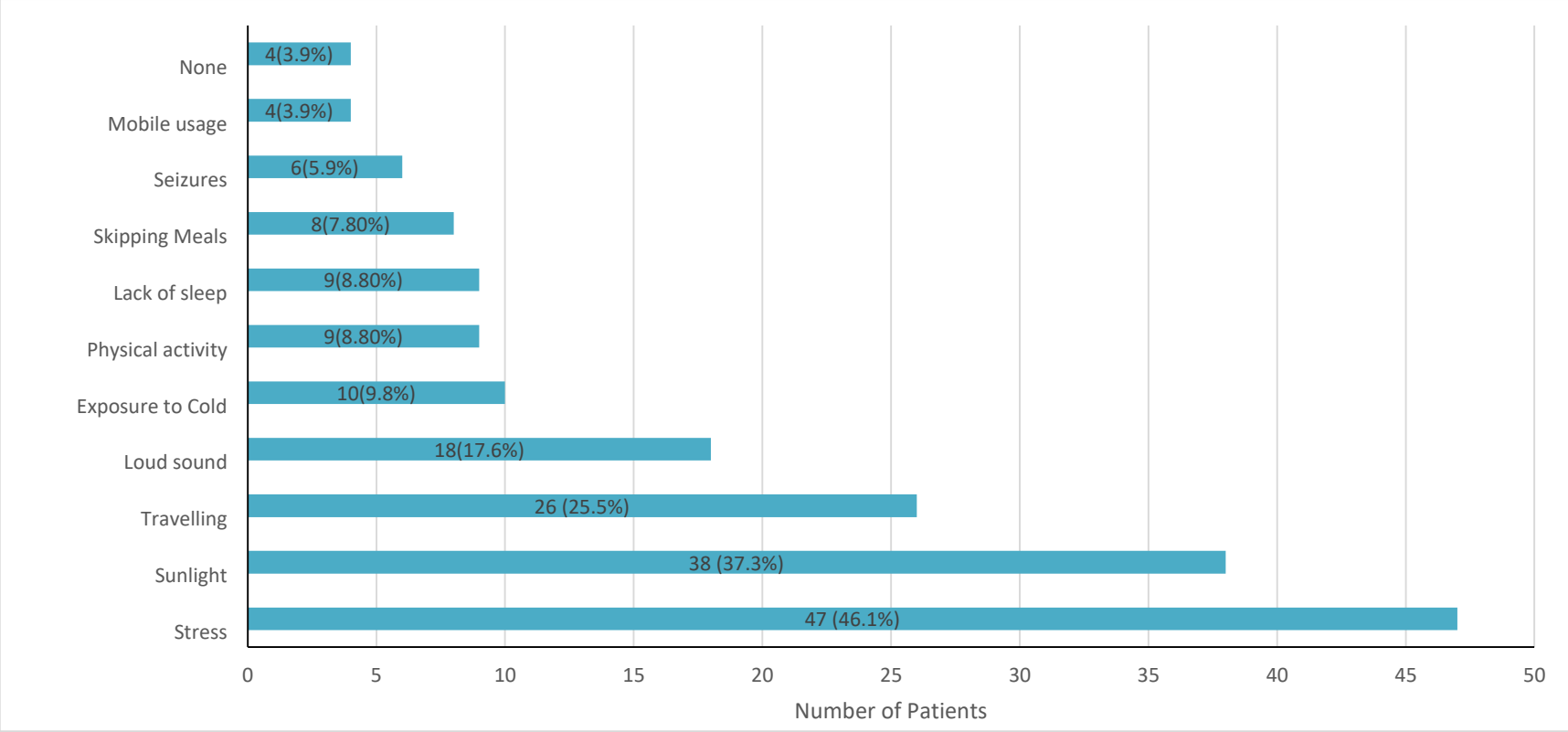


Figure 8

Location of pain

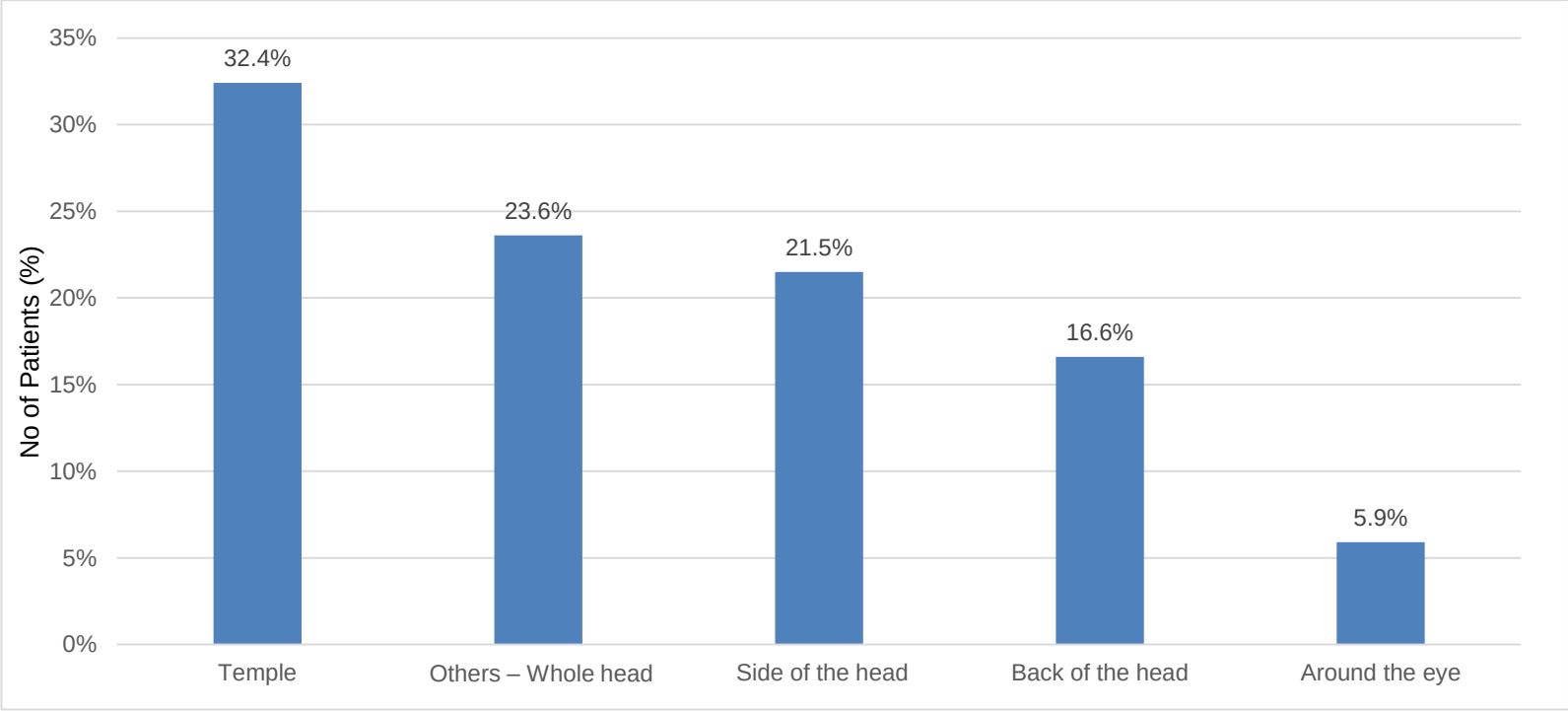


Figure 9

Type of pain

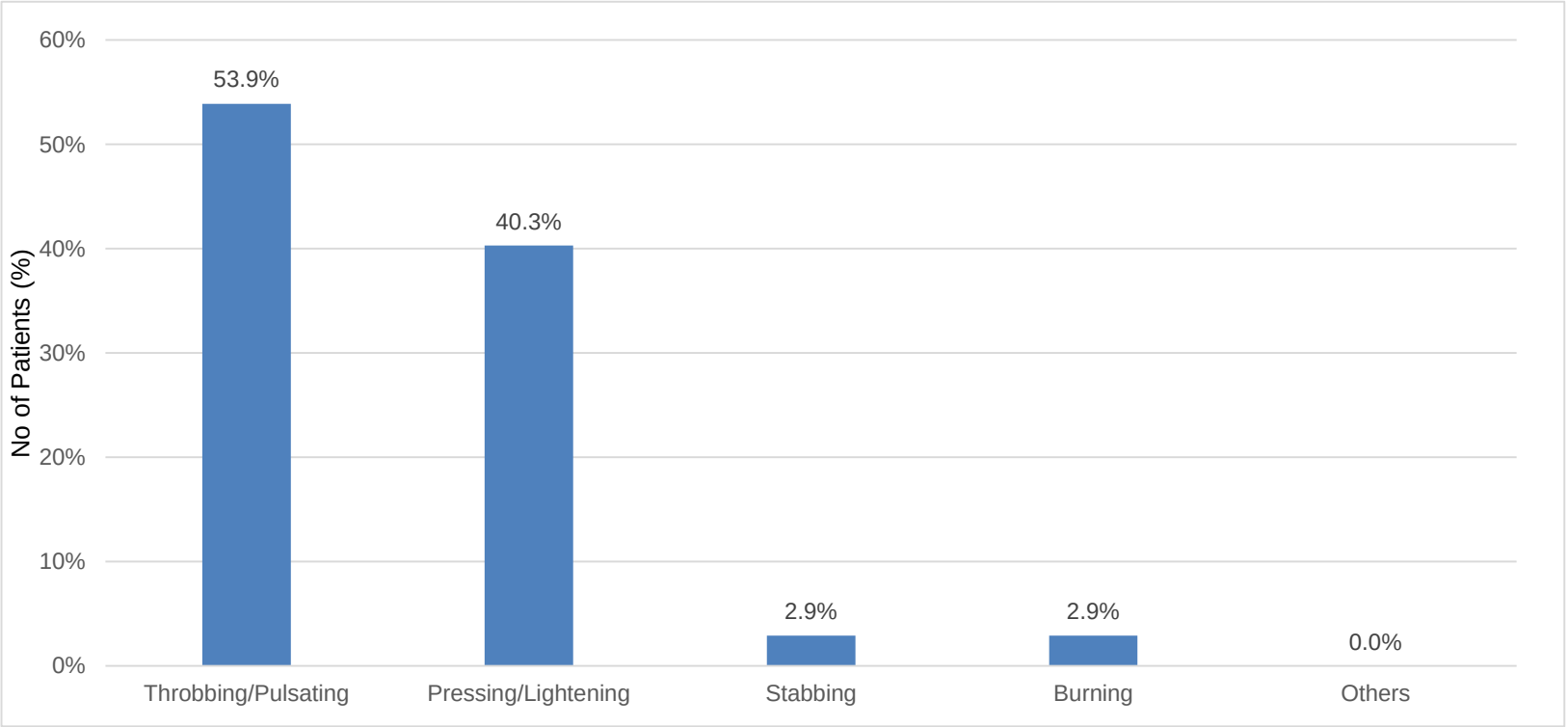


Figure 10

Symptoms occurring along with headache

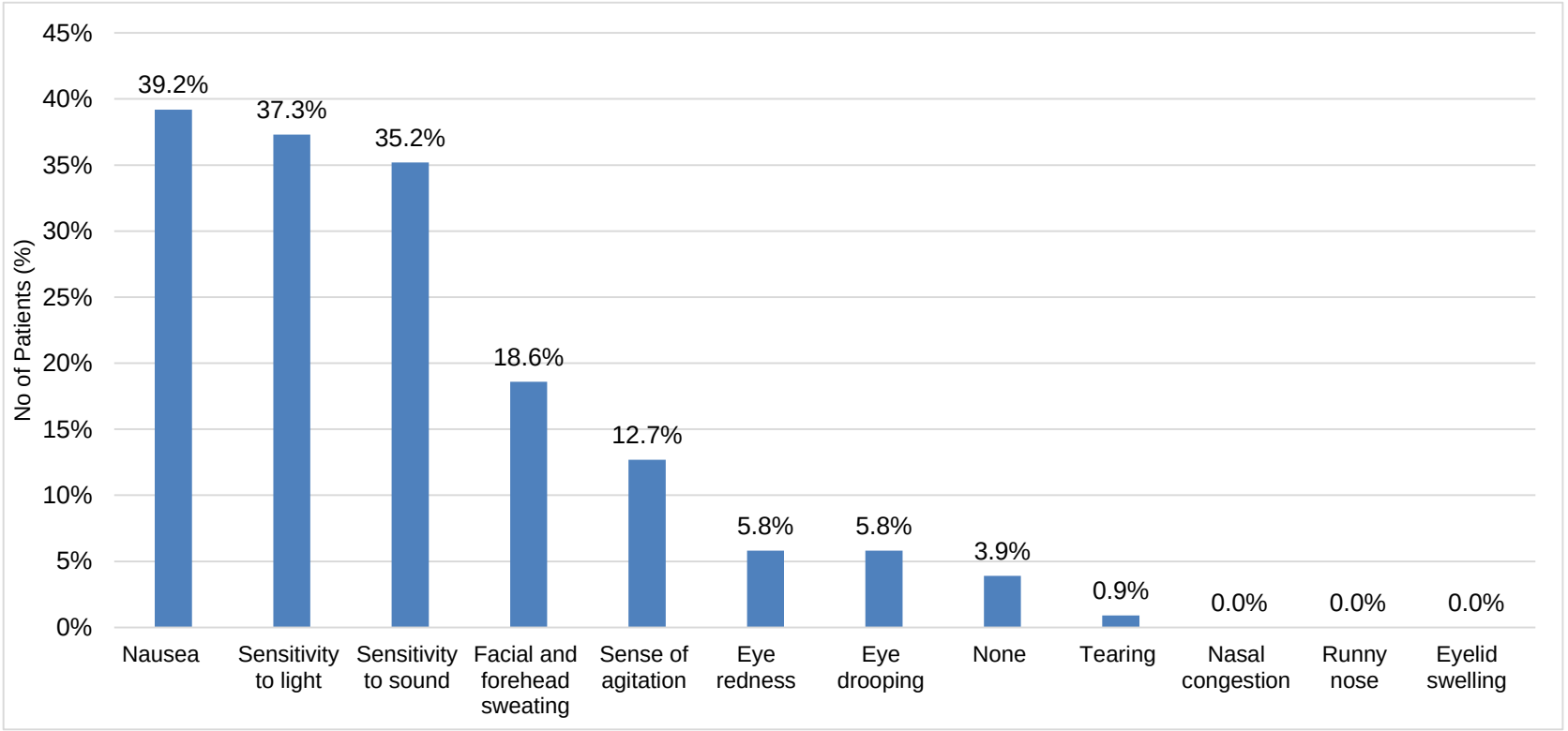


Figure 11

Various neurological symptoms associated with migraine (n=32)

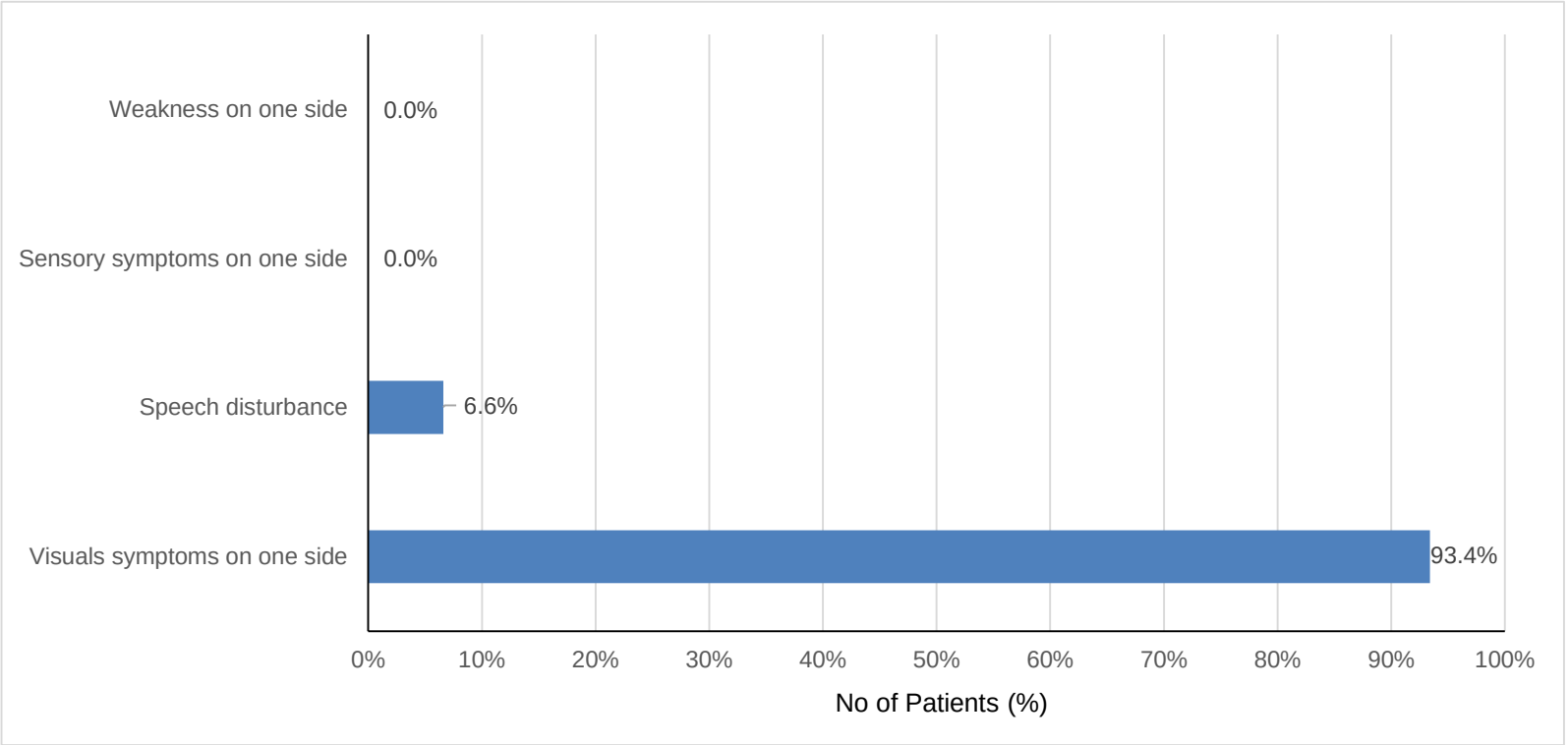


Figure 12

Factors responsible for migraine attack

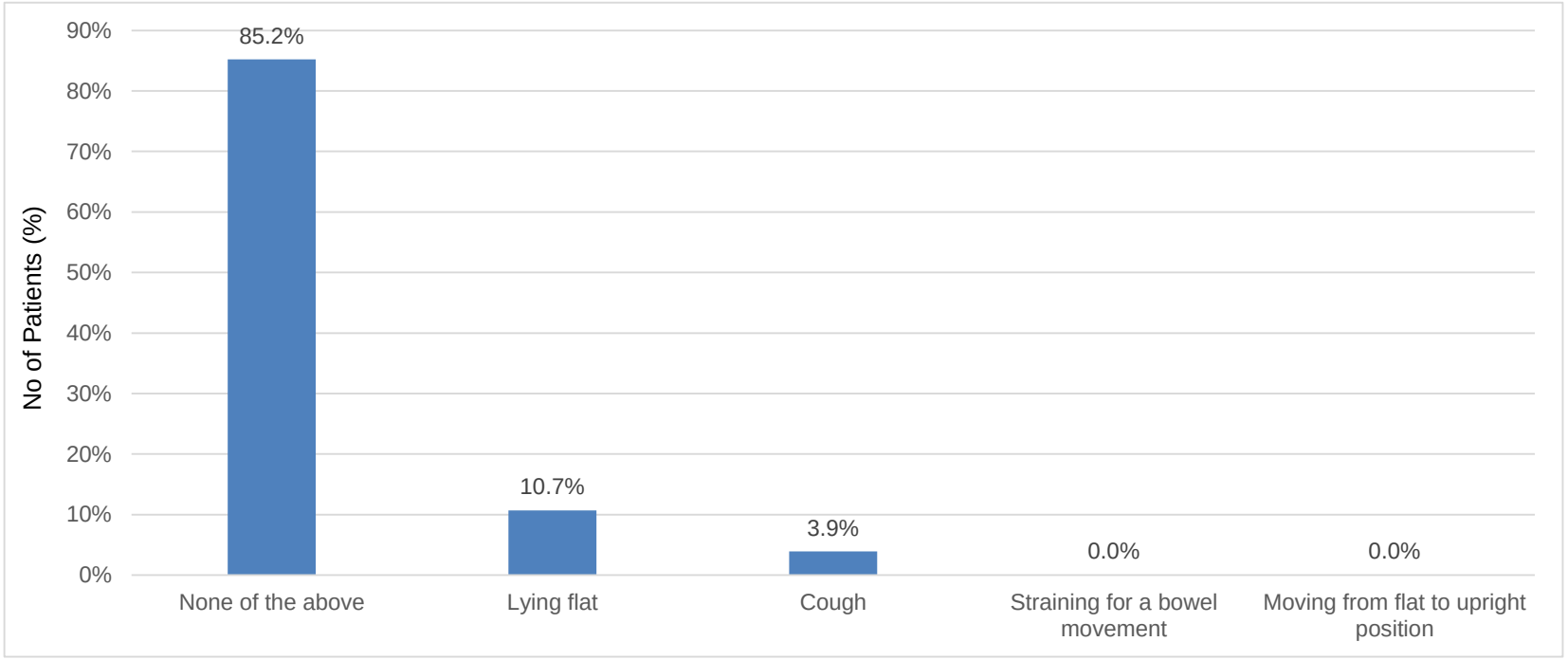


Figure 13

Self-medications used to relieve an acute attack

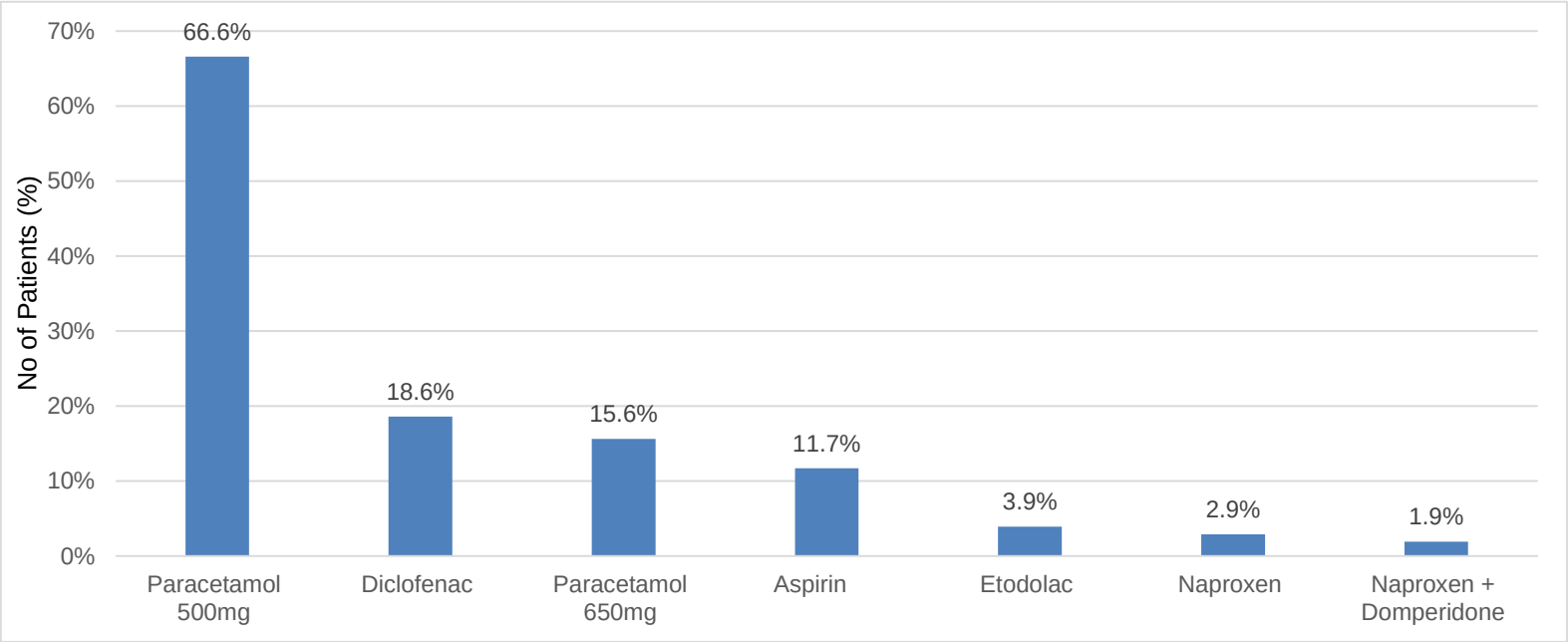


Table 1

Distribution of patients based on AED alone and dose in Patients with migraine and GTCS.

Sr. No.	AED used	Dose	No of patients
1	VPA	20-25mg/kg	18
2	LEV	15-20mg/kg	15
		8mg/kg	1
3	CBZ	20mg/kg	3
4	OXC	900-1200 mg/day	2
5	PHT	400mg/day	1
6	LAC	350mg/kg	1
7	BRV	100mg/day	1
Total			42

Figure 14

AED used alone and mean frequency of migraine in patients with GTCS (n=42)

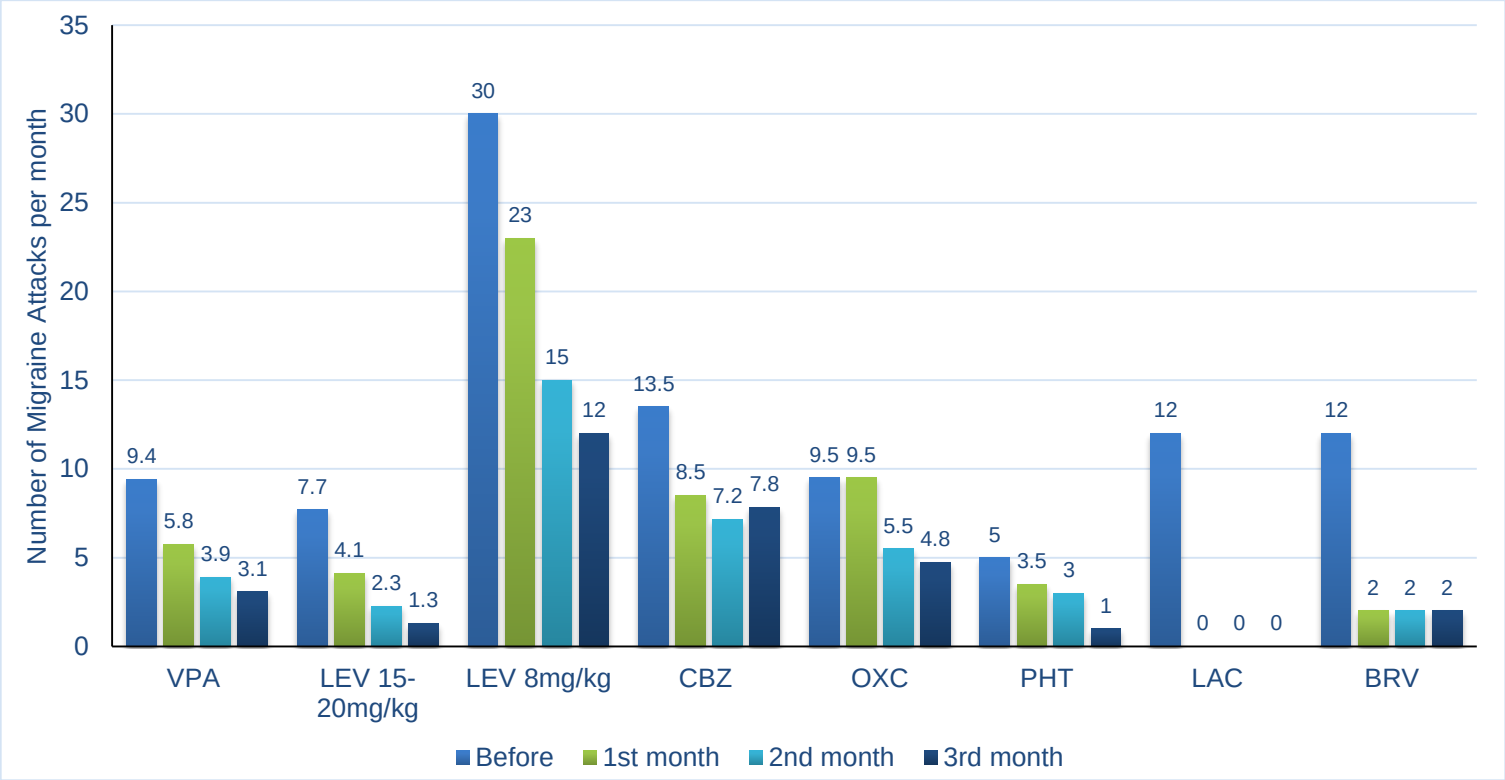


Table 2

Frequency of migraine attacks with VPA 20-25mg/kg

Groups	Mean ± SD
Before	9.42 ± 8.66
1st month	5.75 ± 7.05
2nd month	3.92 ± 6.96
3rd month	3.03 ± 7.07

Groups		Mean Difference	Std. Error	Significance
Before	1st month	3.667	1.791	0.056
	2nd month	5.500*	1.752	0.006
	3rd month	6.333*	1.809	0.003
1st month	Before	-3.667	1.791	0.056
	2nd month	1.833*	0.441	0.001
	3rd month	2.667*	0.833	0.005
2nd month	Before	-5.500*	1.752	0.006
	1st month	-1.833*	0.441	0.001
	3rd month	.833	0.441	0.076
3rd month	Before	-6.333*	1.809	0.003
	1st month	-2.667*	0.833	0.005
	2nd month	-.833	0.441	0.076

Table 3

Frequency of migraine attacks with LEV 15-20mg/kg

Groups	Mean ± SD
Before	7.7 ± 7.9
1st month	4.1 ± 3.3
2nd month	2.3 ± 2.1
3rd month	1.3 ± 1.8

Groups		Mean Difference	Std. Error	Significance
Before	1st month	3.600	1.700	0.053
	2nd month	5.433*	1.831	0.010
	3rd month	6.400*	1.991	0.006
1st month	Before	-3.600	1.700	0.053
	2nd month	1.833*	0.454	0.001
	3rd month	2.800*	0.672	0.001
2nd month	Before	-5.433*	1.831	0.010
	1st month	-1.833*	0.454	0.001
	3rd month	0.967*	0.421	0.038
3rd month	Before	-6.400*	1.991	0.006
	1st month	-2.800*	0.672	0.001
	2nd month	-0.967*	0.421	0.038

Figure 15

AED used alone and mean VAS score for migraine in patients with GTCS (n=42)

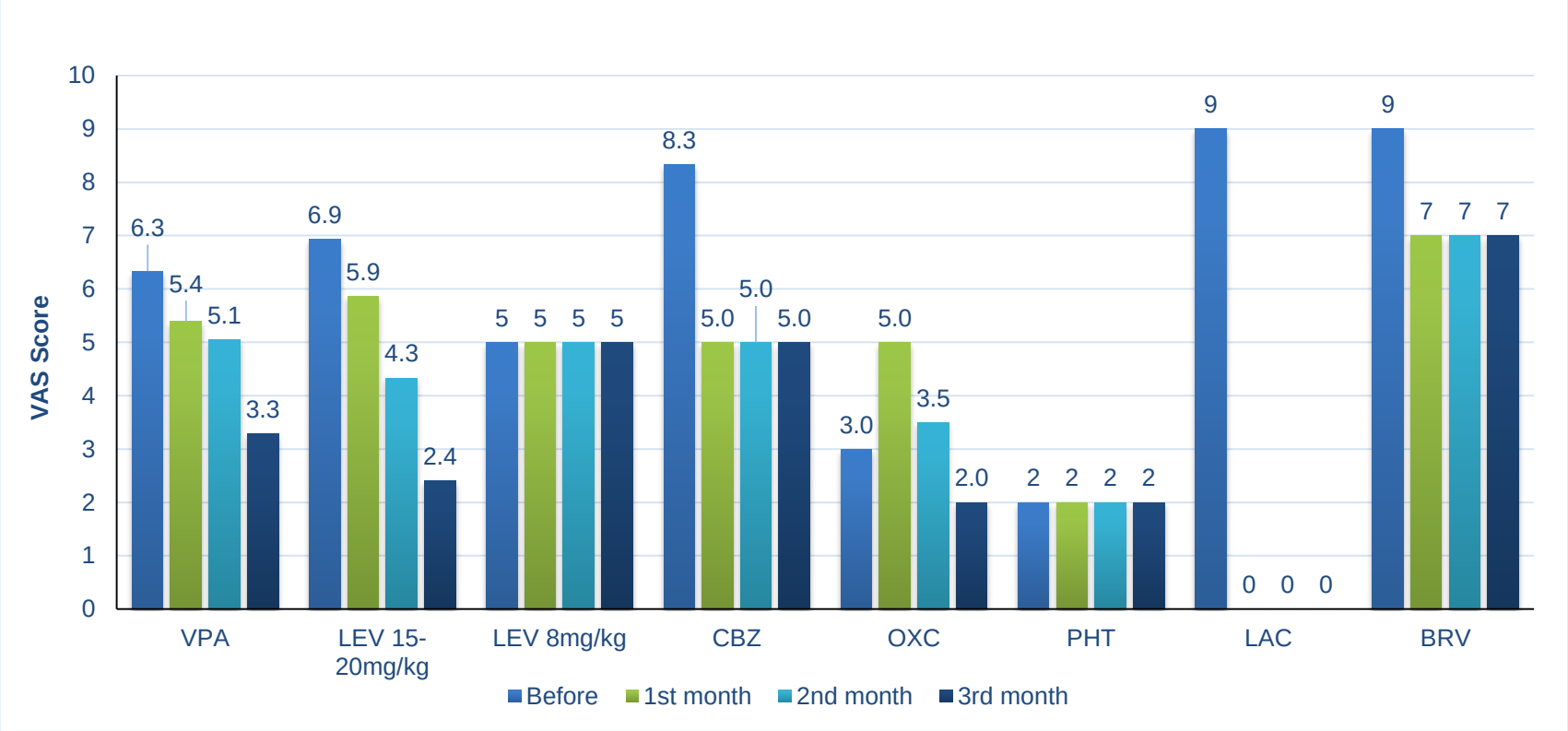


Table 4

Mean VAS score with VPA 20-25mg/kg

Groups	Mean ± SD
Before	6.33 ± 2.20
1st month	5.39 ± 2.52
2nd month	5.06 ± 2.39
3rd month	3.23 ± 3.23

Groups		Mean Difference	Std. Error	Significance
Before	1st month	0.944	0.574	0.118
	2nd month	1.278*	0.587	0.044
	3rd month	3.056*	0.752	0.001
1st month	Before	-0.944	0.574	0.118
	2nd month	0.333	0.162	0.055
	3rd month	2.111*	0.666	0.006
2nd month	Before	-1.278*	0.587	0.044
	1st month	-0.333	0.162	0.055
	3rd month	1.778*	0.597	0.008
3rd month	Before	-3.056*	0.752	0.001
	1st month	-2.111*	0.666	0.006
	2nd month	-1.778*	0.597	0.008

Table 5

Mean VAS score with LEV 15-20mg/kg – VAS

Groups	Mean ± SD
Before	6.9 ± 1.8
1st month	5.9 ± 2.4
2nd month	4.3 ± 3.0
3rd month	2.4 ± 3.2

Groups		Mean Difference	Std. Error	Significance
Before	1st month	1.067	0.658	0.127
	2nd month	2.600*	0.761	0.004
	3rd month	4.533*	0.761	0.000
1st month	Before	-1.067	0.658	0.127
	2nd month	1.533*	0.631	0.029
	3rd month	3.467*	0.792	0.001
2nd month	Before	-2.600*	0.761	0.004
	1st month	-1.533*	0.631	0.029
	3rd month	1.933*	0.765	0.024
3rd month	Before	-4.533*	0.761	0.000
	1st month	-3.467*	0.792	0.001
	2nd month	-1.933*	0.765	0.024

FIGURE 16

AED USED & MEAN GAMS SCORE FOR MIGRAINE IN PATIENTS WITH GTCS (N=42)

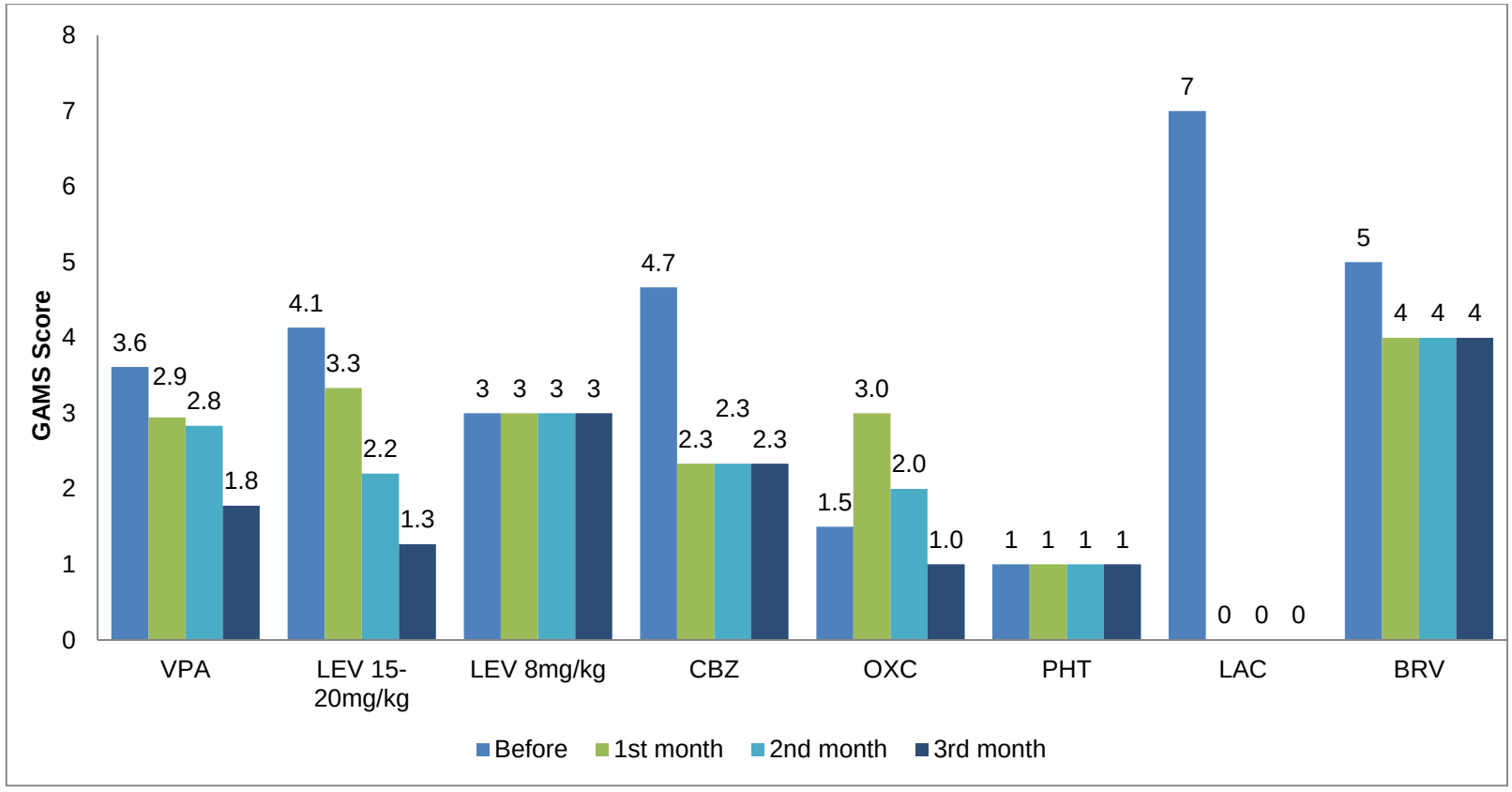


Table 6

Mean GAMS score with VPA 20-25 mg/kg

Groups	Mean ± SD
Before	3.61 ± 1.46
1st month	2.94 ± 1.59
2nd month	2.83 ± 1.54
3rd month	1.78 ± 1.90

Groups		Mean Difference	Std. Error	Significance
Before	1st month	0.667	0.362	0.083
	2nd month	0.778*	0.358	0.044
	3rd month	1.833*	0.452	0.001
1st month	Before	-0.667	0.362	0.083
	2nd month	0.111	0.076	0.163
	3rd month	1.167*	0.406	0.011
2nd month	Before	-0.778*	0.358	0.044
	1st month	-0.111	0.076	0.163
	3rd month	1.056*	0.366	0.010
3rd month	Before	-1.833*	0.452	0.001
	1st month	-1.167*	0.406	0.011
	2nd month	-1.056*	0.366	0.010

Table 7

Mean GAMS score with LEV 15-20mg/kg

Groups	Mean ± SD
Before	4.1 ± 1.4
1st month	3.3 ± 1.7
2nd month	2.2 ± 1.6
3rd month	1.3 ± 1.8

Groups		Mean Difference	Std. Error	Significance
Before	1st month	0.800	0.470	0.111
	2nd month	1.933*	0.483	0.001
	3rd month	2.867*	0.456	0.000
1st month	Before	-0.800	0.470	0.111
	2nd month	1.133*	0.413	0.016
	3rd month	2.067*	0.463	0.001
2nd month	Before	-1.933*	0.483	0.001
	1st month	-1.133*	0.413	0.016
	3rd month	0.933*	0.371	0.025
3rd month	Before	-2.867*	0.456	0.000
	1st month	-2.067*	0.463	0.001
	2nd month	-0.933*	0.371	0.025

Table 8

Distribution of patients based on AED + Propranolol and dose in patients with migraine and GTCS.

Sr. No.	AED + Propanolol	No of patients
1	VPA 20-25mg/kg + Propranolol 10mg/day	4
2	LEV 15-20mg/kg + Propranolol 10mg/day	3
3	PHT 400mg/kg + Propranolol 10mg/day	1
4	LAC 350mg/day + Propranolol 10mg/day	1
Total		9

FIGURE 17

AED+ PROPRANOLOL USED AND MEAN FREQUENCY OF MIGRAINE IN PATIENTS WITH GTCS (N=9)

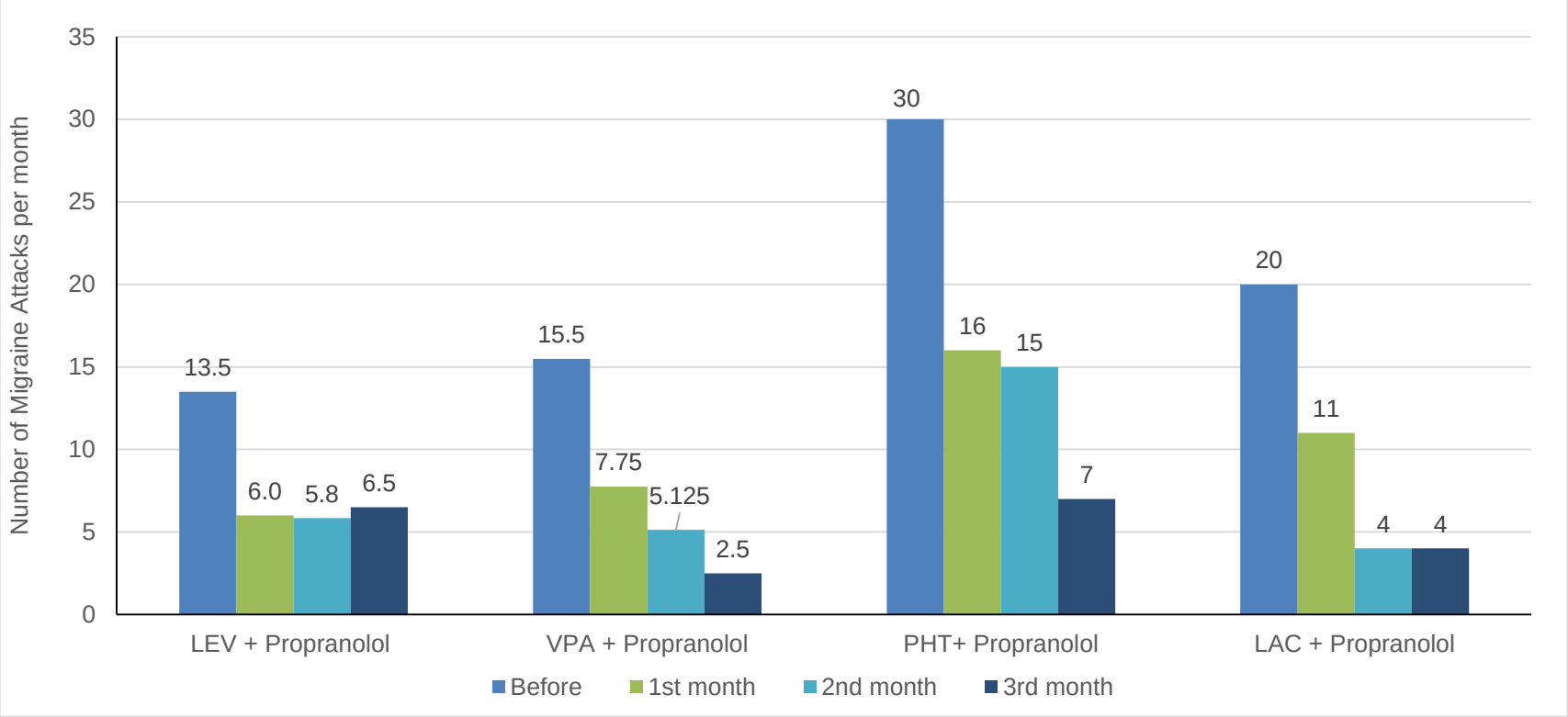


Figure 18

AED + Propranolol used and mean VAS of migraine in patients with GTCS (N=9)

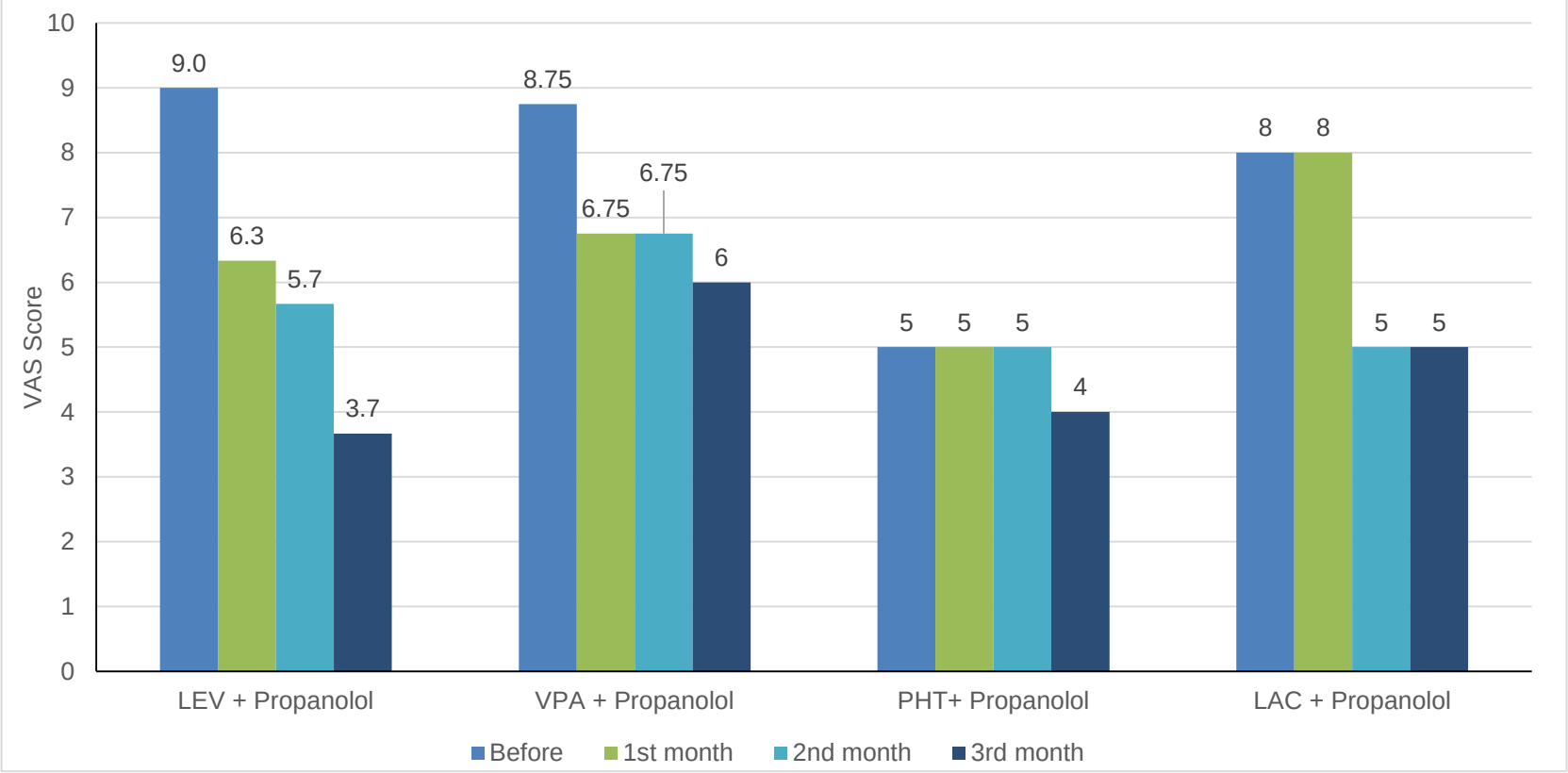


Figure 19

AED+ Propranolol used and mean GAMS of migraine in patients with GTCS (N=9)

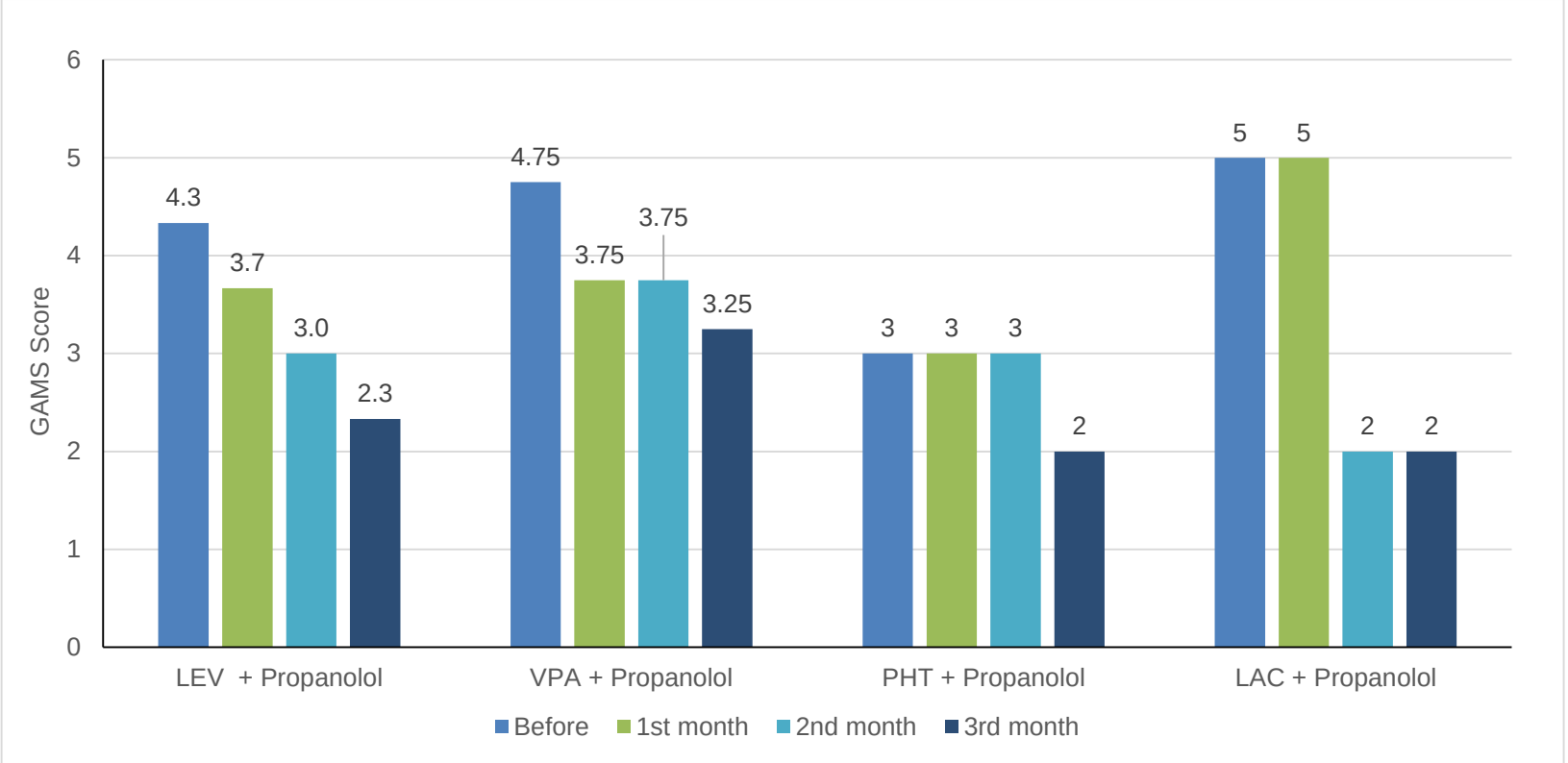


Table 9

Distribution of patients based on AED and dose in patients with migraine and CPS

Sr. No.	AED used	Dose	No of patients
1	LEV	15-20mg/kg	4
		8mg/kg	1
2	OXC	900-1200 mg/day	4
3	CBZ	15-20mg/kg	2
4	VPA	25mg/kg	1
5	LAC	350mg/day	1
Total			13

Figure 20

AED used alone and mean frequency of migraine in patients with complex partial seizures (N=13)

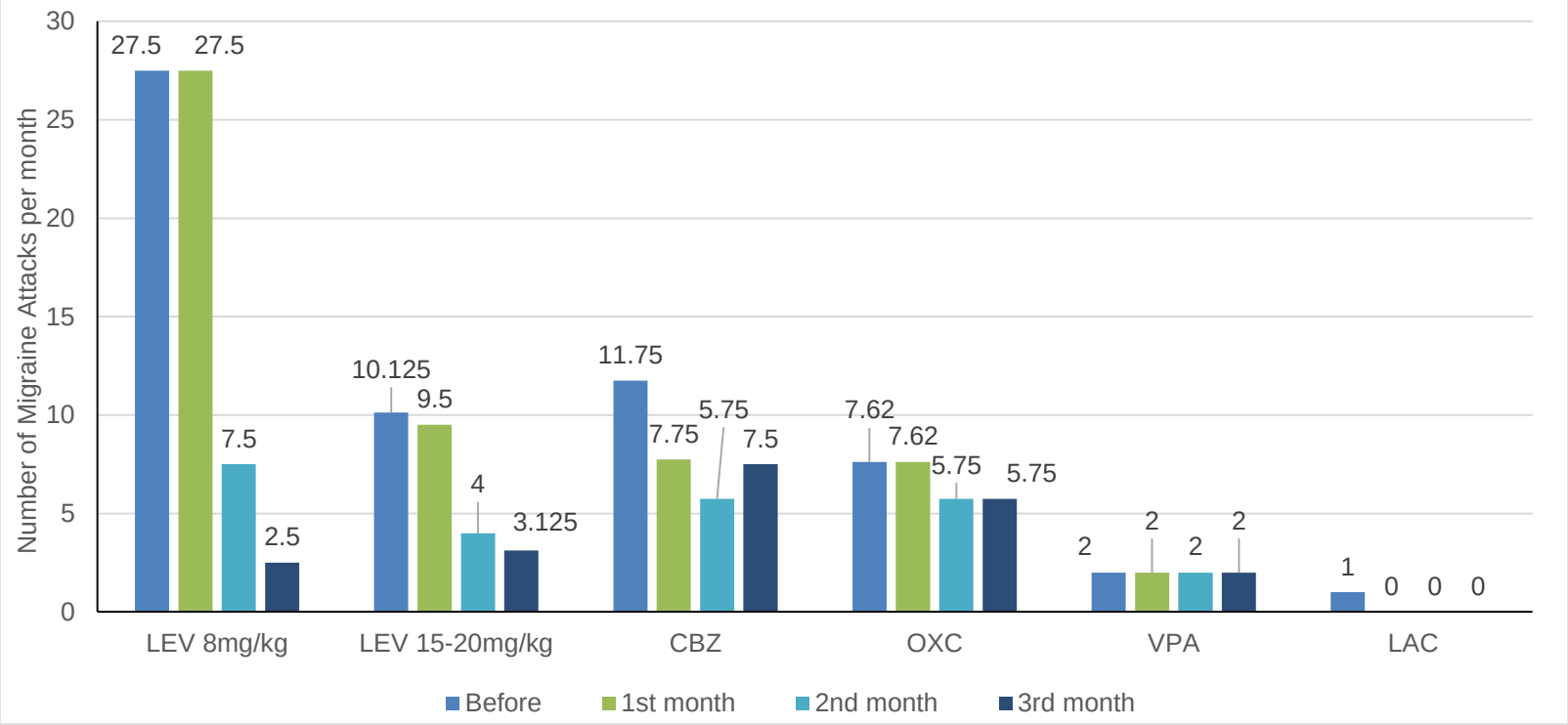


Figure 21

AED used alone and mean VAS of migraine in patients with complex partial seizures (N=13)

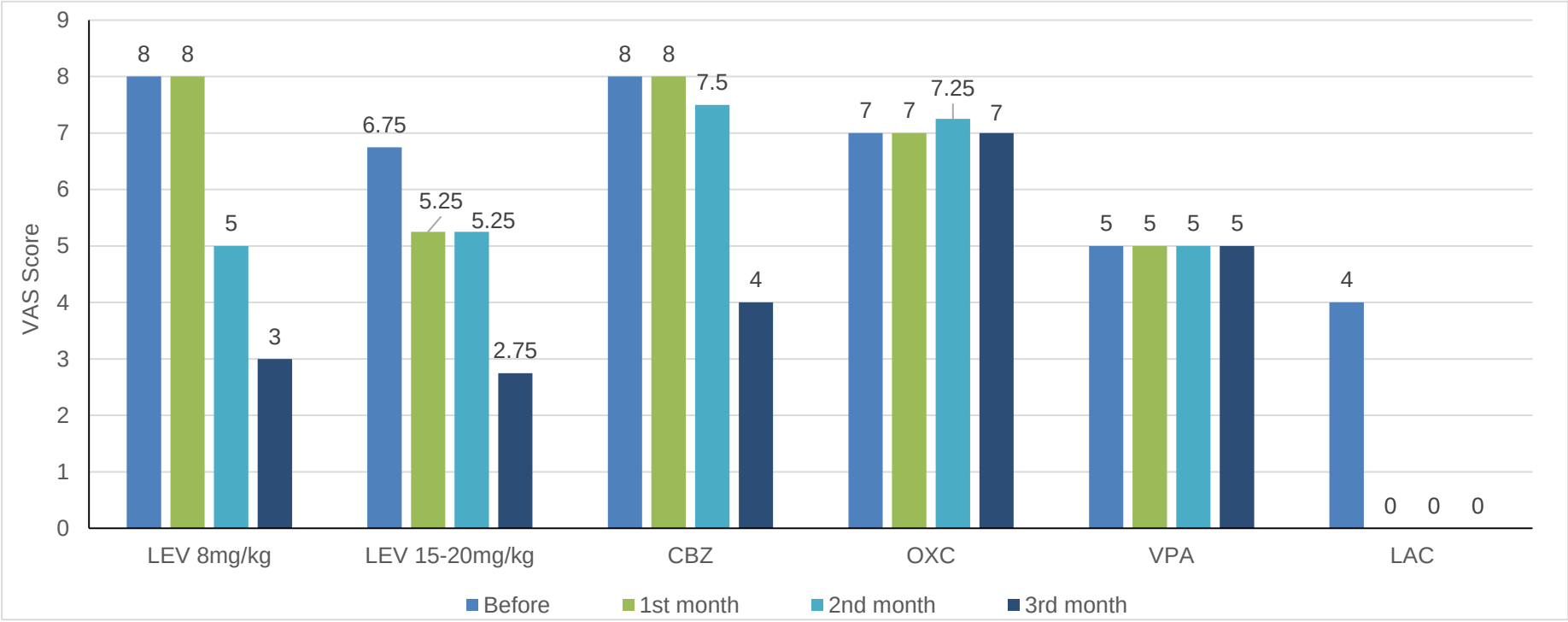


Figure 22

AED used alone and mean GAMS of migraine in patients with complex partial seizures (N=13)

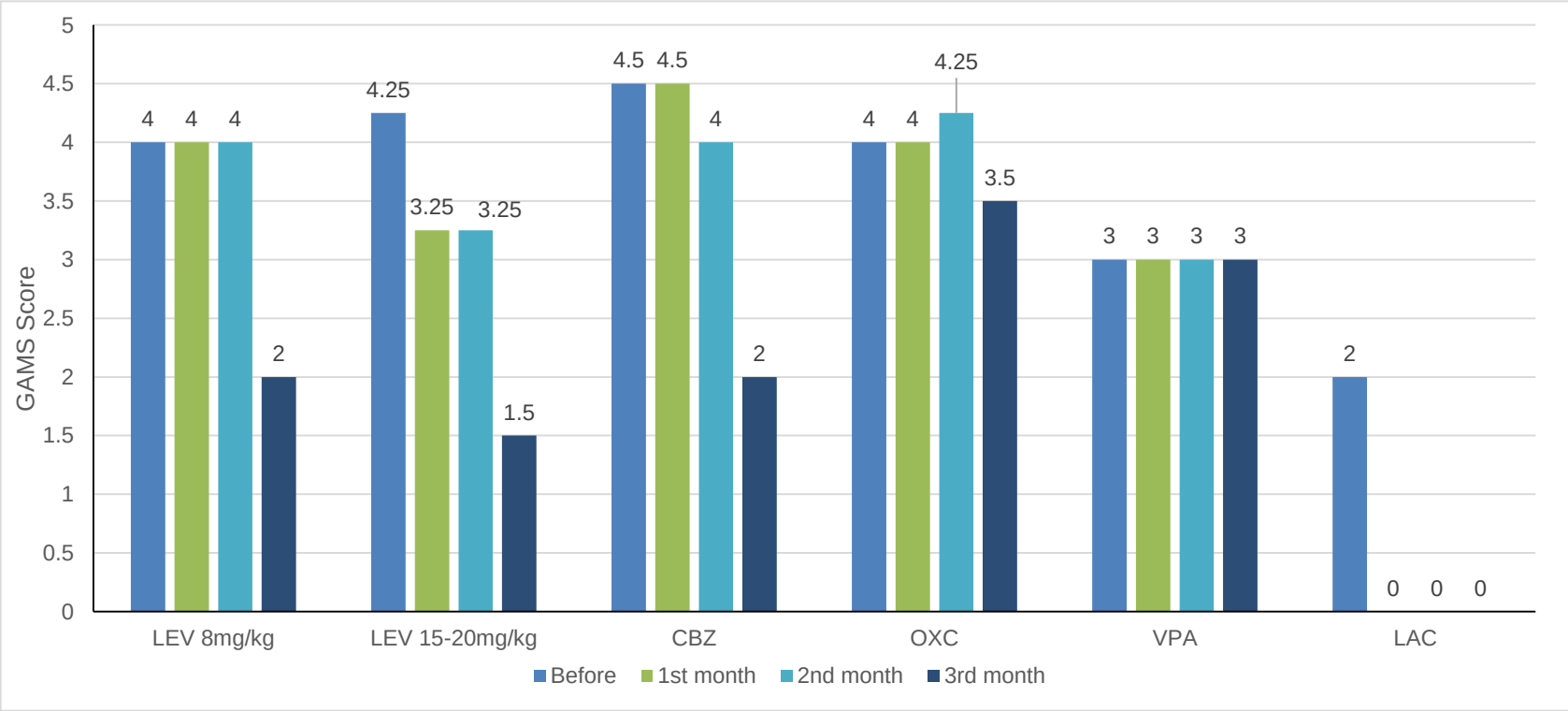


Table 10

Distribution of patients based on AED + Propranolol and dose in patients with migraine and CPS

Sr. No.	AED + Propanolol	No of patients
1	LEV 20mg/kg + Propranolol 10mg/day	1
2	LEV 8mg/kg + Propranolol 10mg/day	1
3	OXC 1200mg/day + Propranolol 10mg/day	1
Total		3

Figure 23

AED+ Propranolol used and mean frequency of migraine in patients with complex partial seizures (N=3)

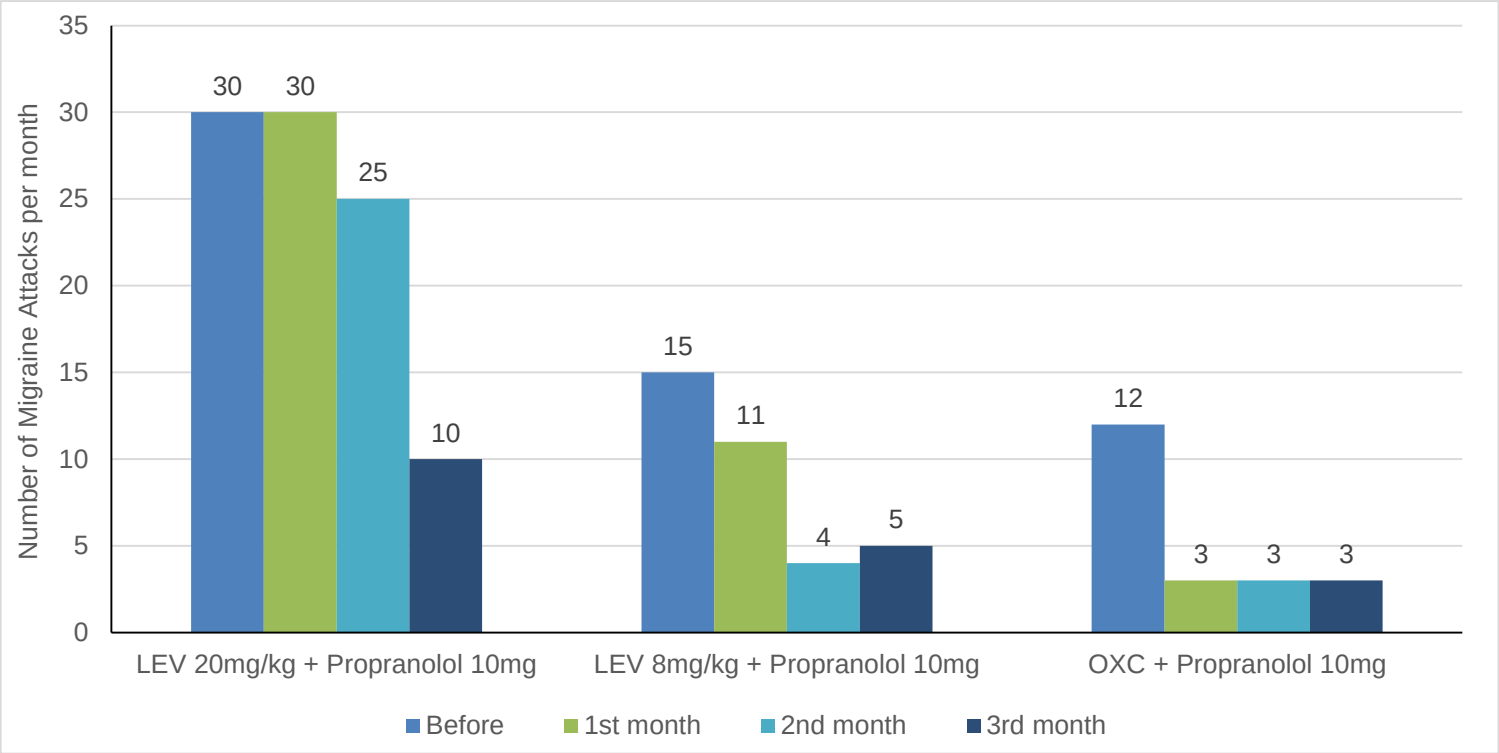


Figure 24

AED+ Propranolol used and mean VAS of migraine in patients with complex partial seizures (N=3)

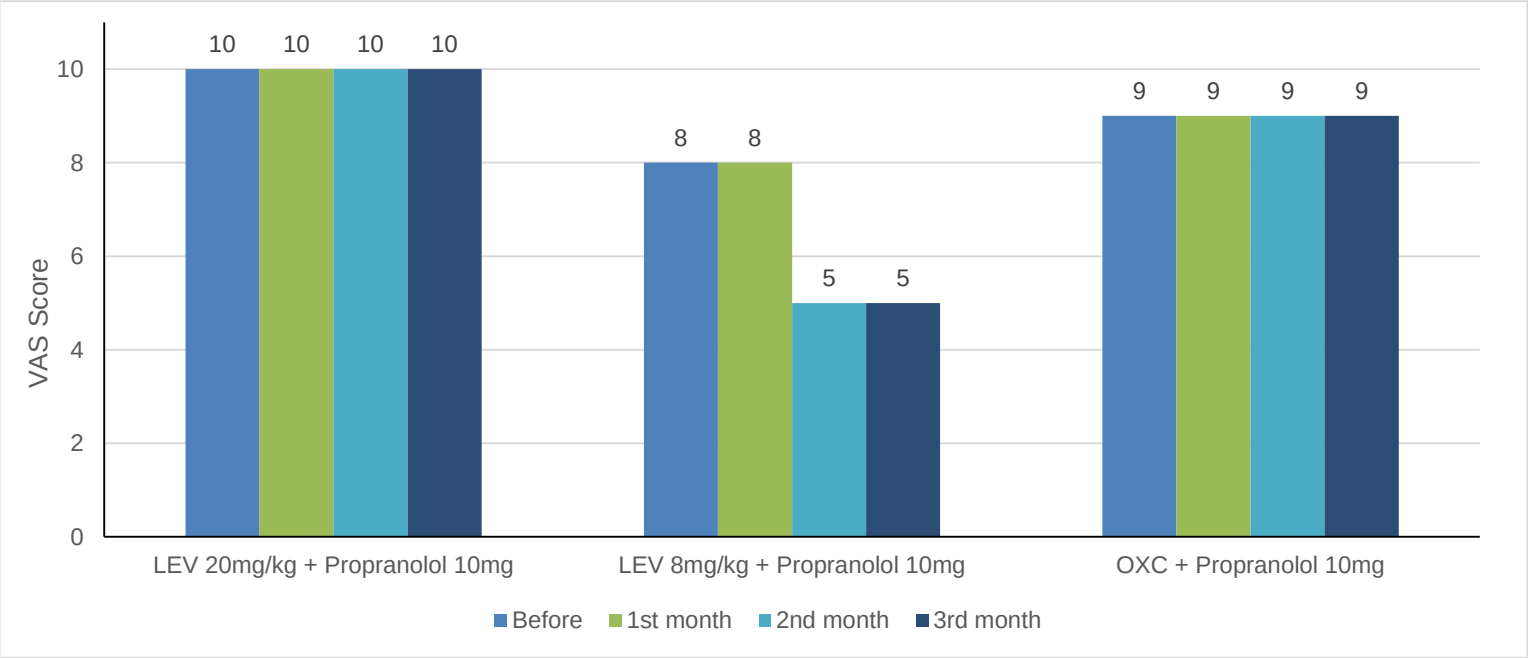


Figure 25

AED+ Propranolol used and mean GAMS of migraine in patients with complex partial seizures (N=3)

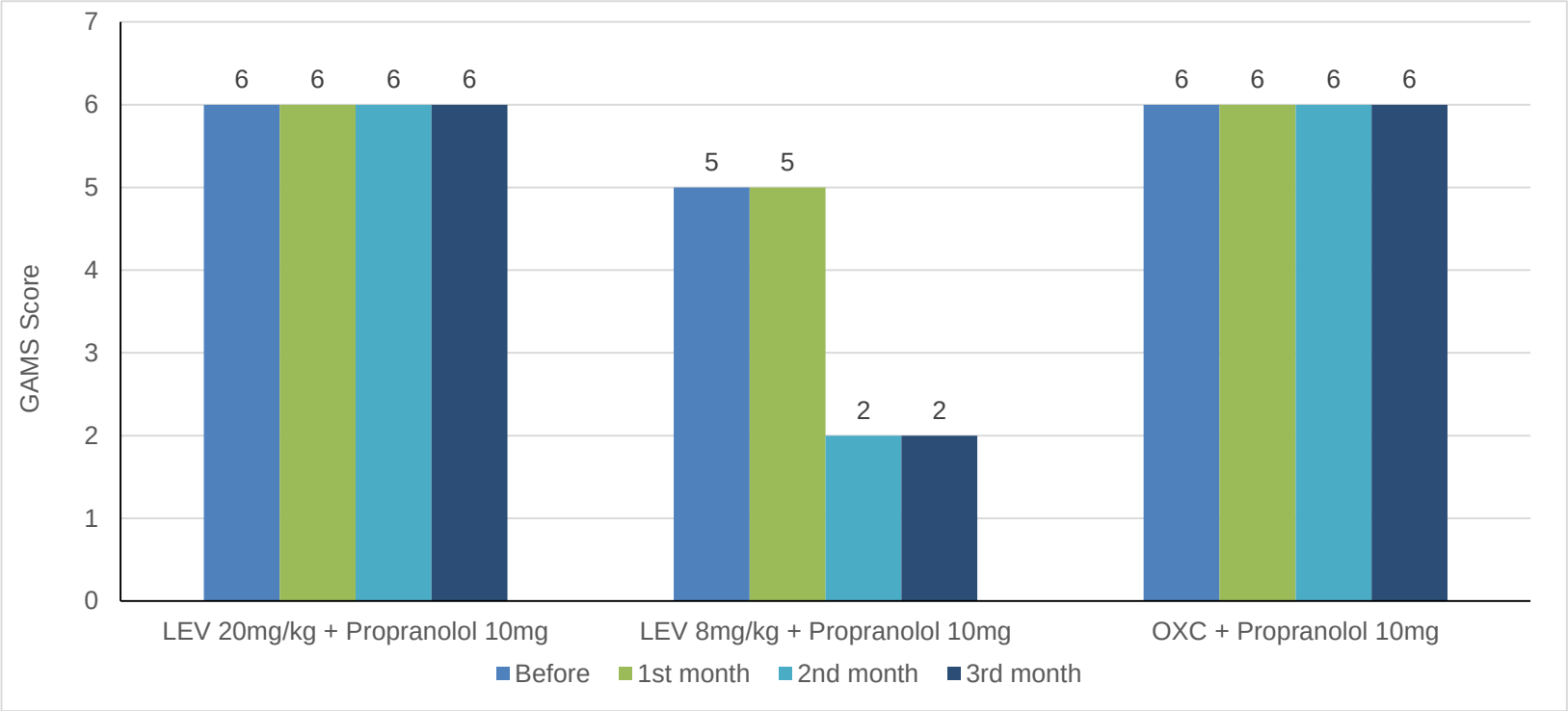


Table 11

Distribution of patients based on AED and dose in patients with migraine and Focal seizure.

Sr. No.	AED used	Dose	No. of patients
1	LEV	15-20mg/kg	4
		8mg/kg	2
2	OXC	1000-1050mg/day	2
3	LAC	350mg/day	2
4	CBZ	20mg/kg	1
Total			11

Figure 26

AED used alone and mean frequency of migraine in patients with focal seizures (N=11)

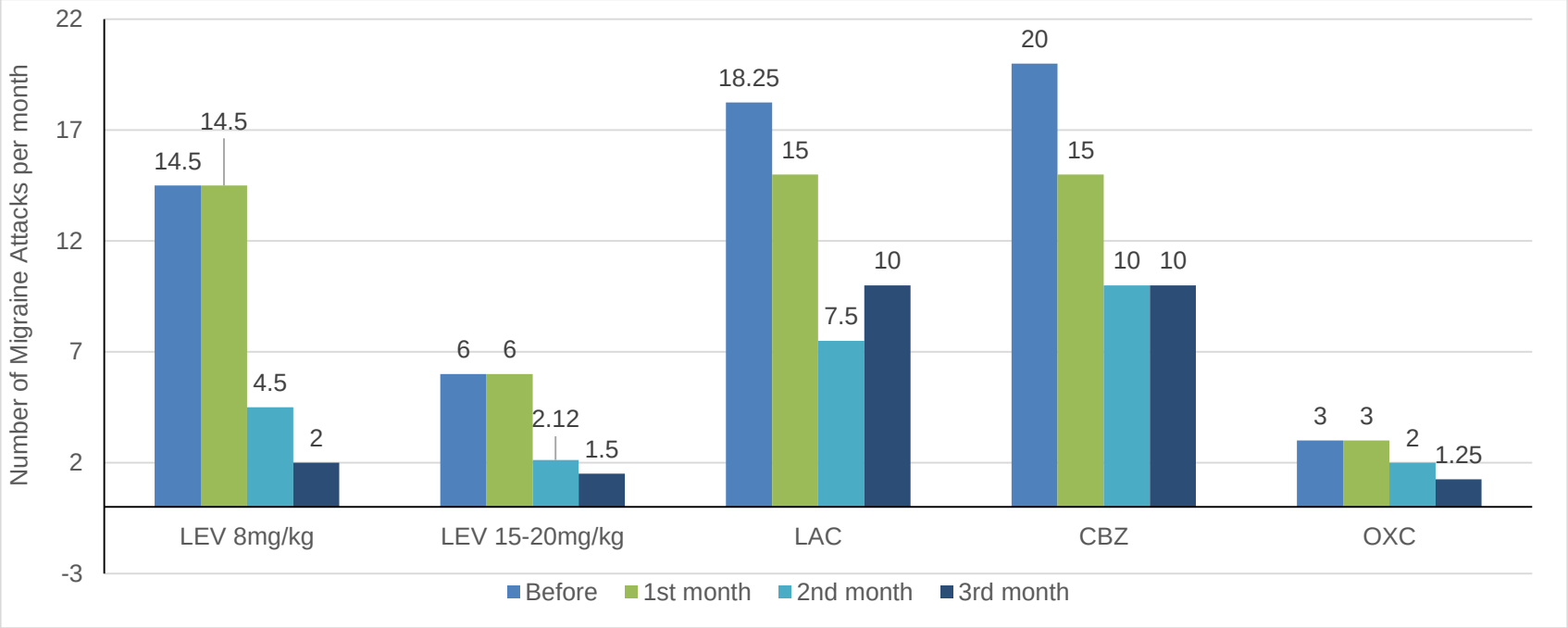


Figure 27

AED used alone and mean VAS of migraine in patients with focal seizures (N=11)

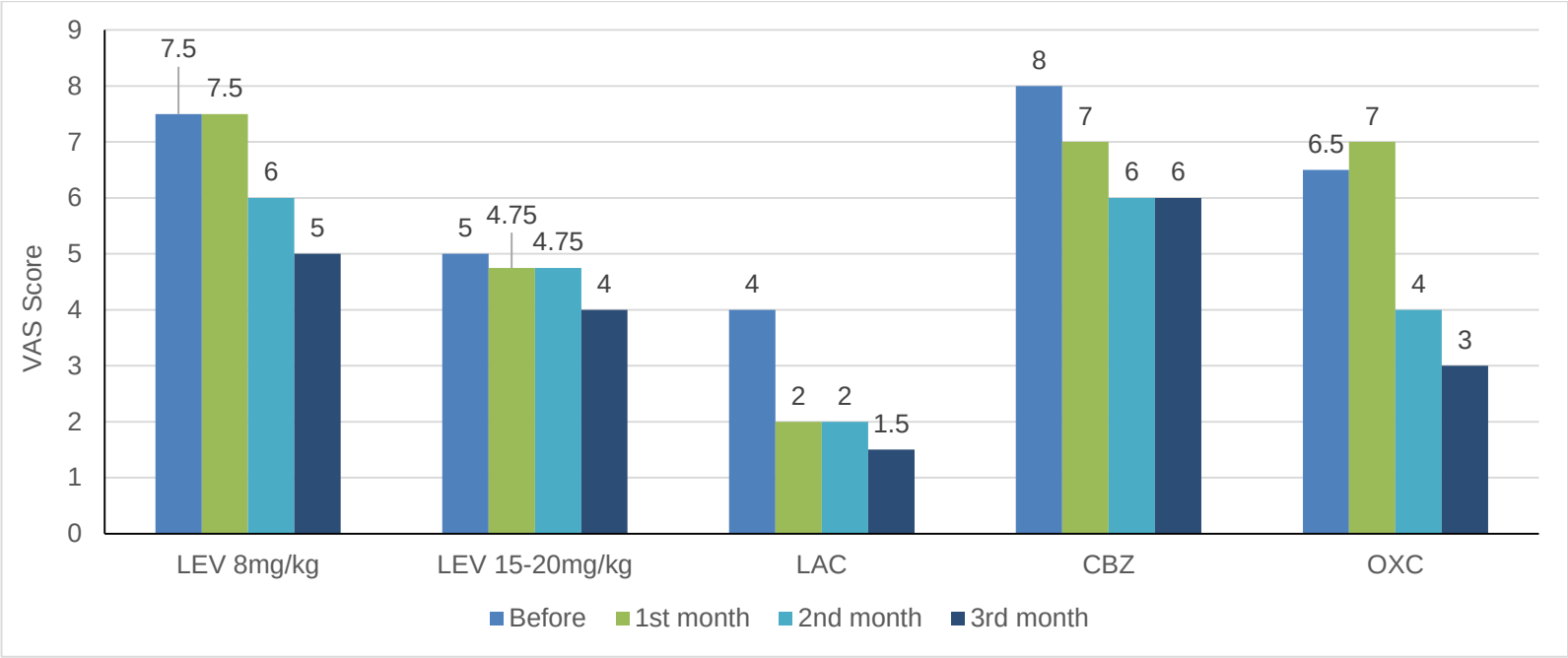


Figure 28

AED used alone and mean GAMS of migraine in patients with focal seizures (N=11)

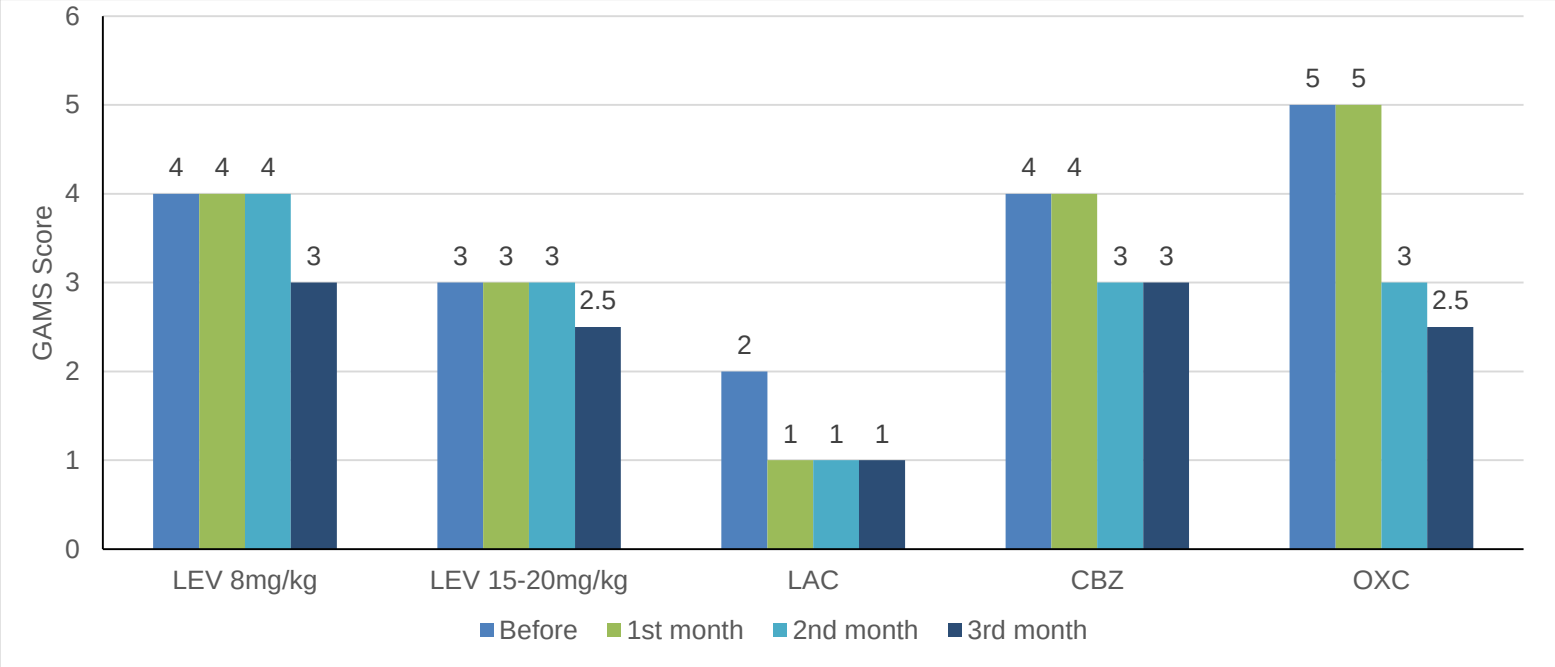


Table 12

Distribution of patients based on AED + Propranolol and dose in patients with migraine and Focal seizures

Sr. No.	AED + Propranolol	No of patients
1	LEV 18mg/kg + Propranolol 10mg	1
2	PHT 350mg/day + Propranolol 10mg	1
Total		2

Figure 29

AED + Propranolol used and mean frequency of migraine in patients with focal seizures (N=2)

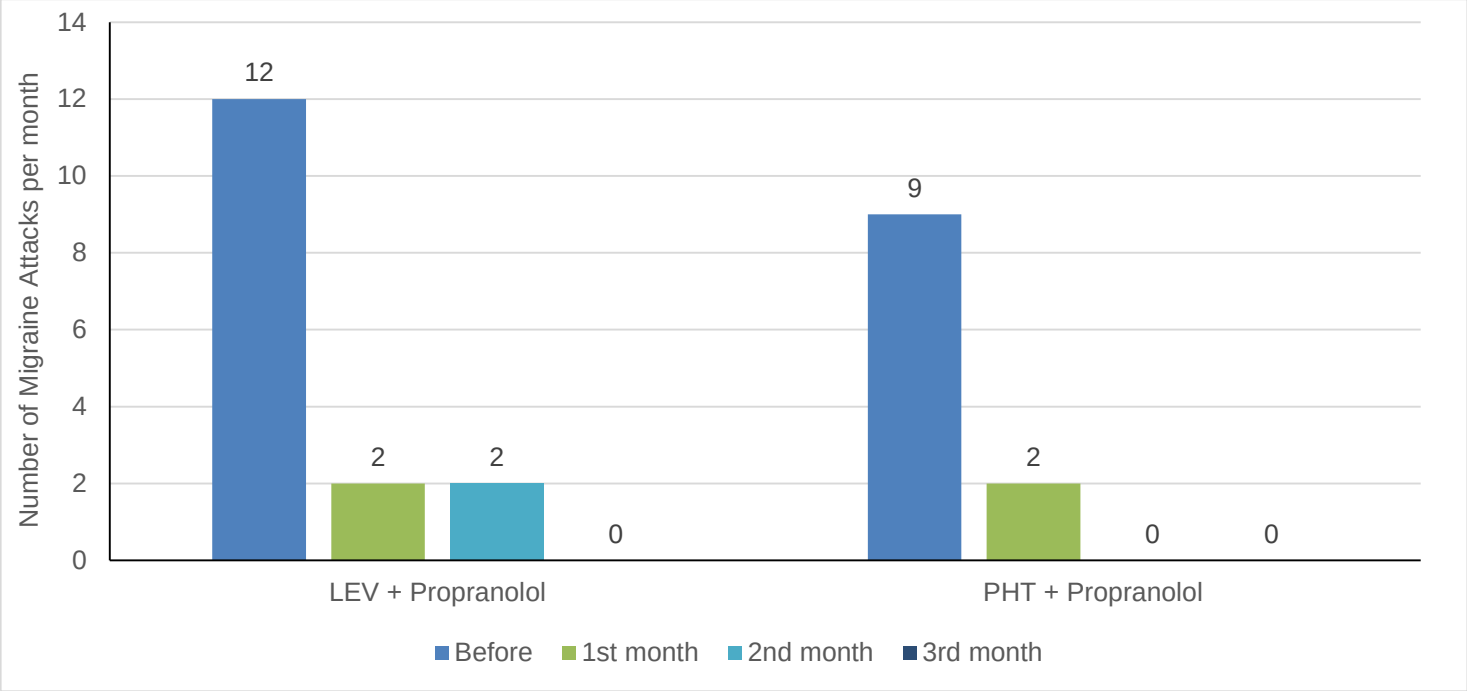


Figure 30

AED + Propranolol used and mean VAS of migraine in patients with focal seizures (N=2)

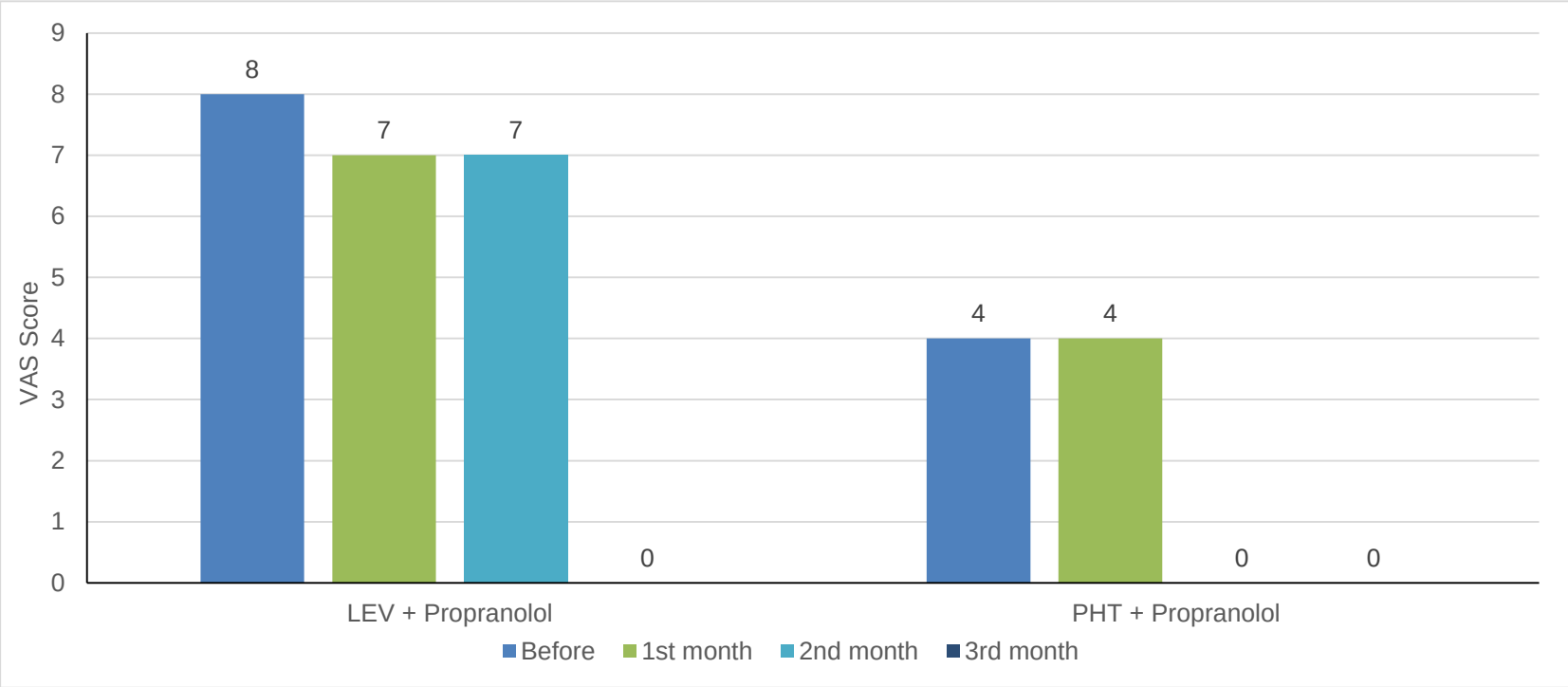


Figure 31

AED + Propranolol used and mean GAMS of migraine in patients with focal seizures (N=2)

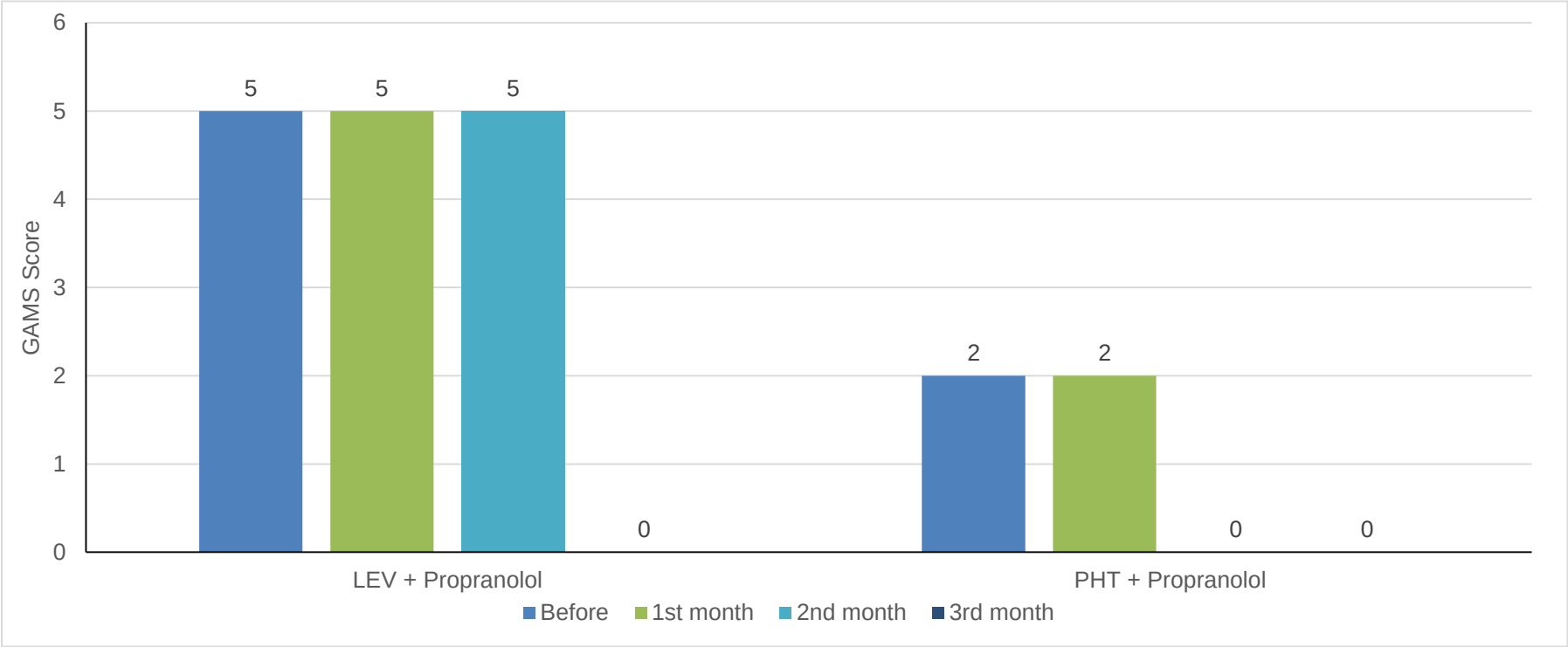


Figure 32

AED used alone and mean frequency of migraine in patients with focal with secondary generalisation (N=4)

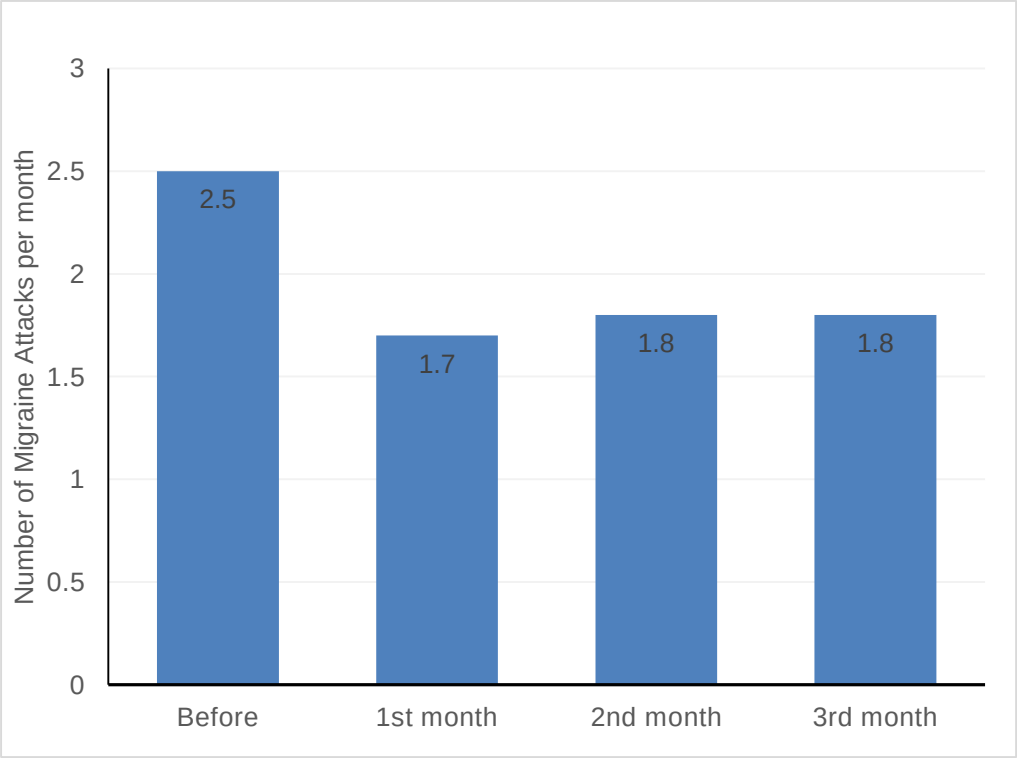


Figure 33

AED used alone and mean VAS score for migraine in patients with focal with secondary generalisation (N=4)

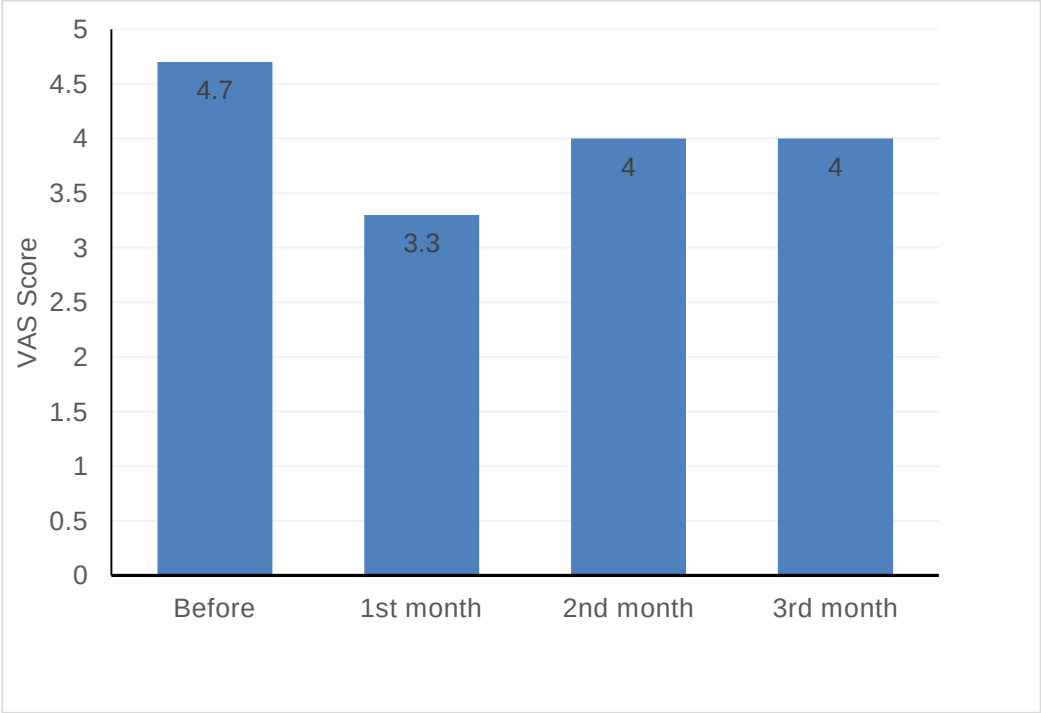


Figure 34

AED used alone & mean GAMS score for migraine in patients with focal with secondary generalisation (N=4)

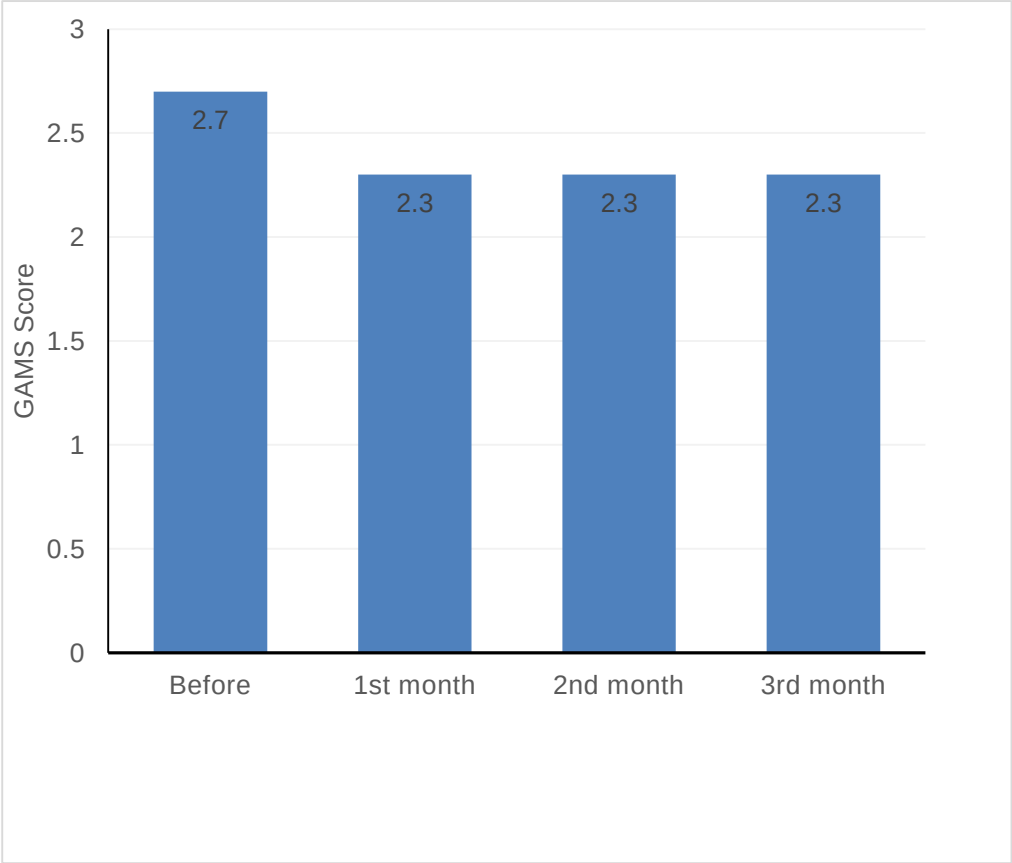


Table 13

Distribution of patients based on AED + Propranolol and dose in patients with migraine and Focal with secondary generalization seizures.

Sr. No.	AED + Propranolol	Noof patients
1	OXC 900-1050mg/kg + Propranolol 10mg/day	2
2	LEV 20mg/kg + Propranolol 10mg/day	1
3	PHT 400mg/day + Propranolol 10mg/day	1
4	BRV 200mg/day + Propranolol 10mg/day	1
Total		5

Figure 35

AED + Propranolol used and mean frequency of migraine in patients with focal with secondary generalization (N=5)

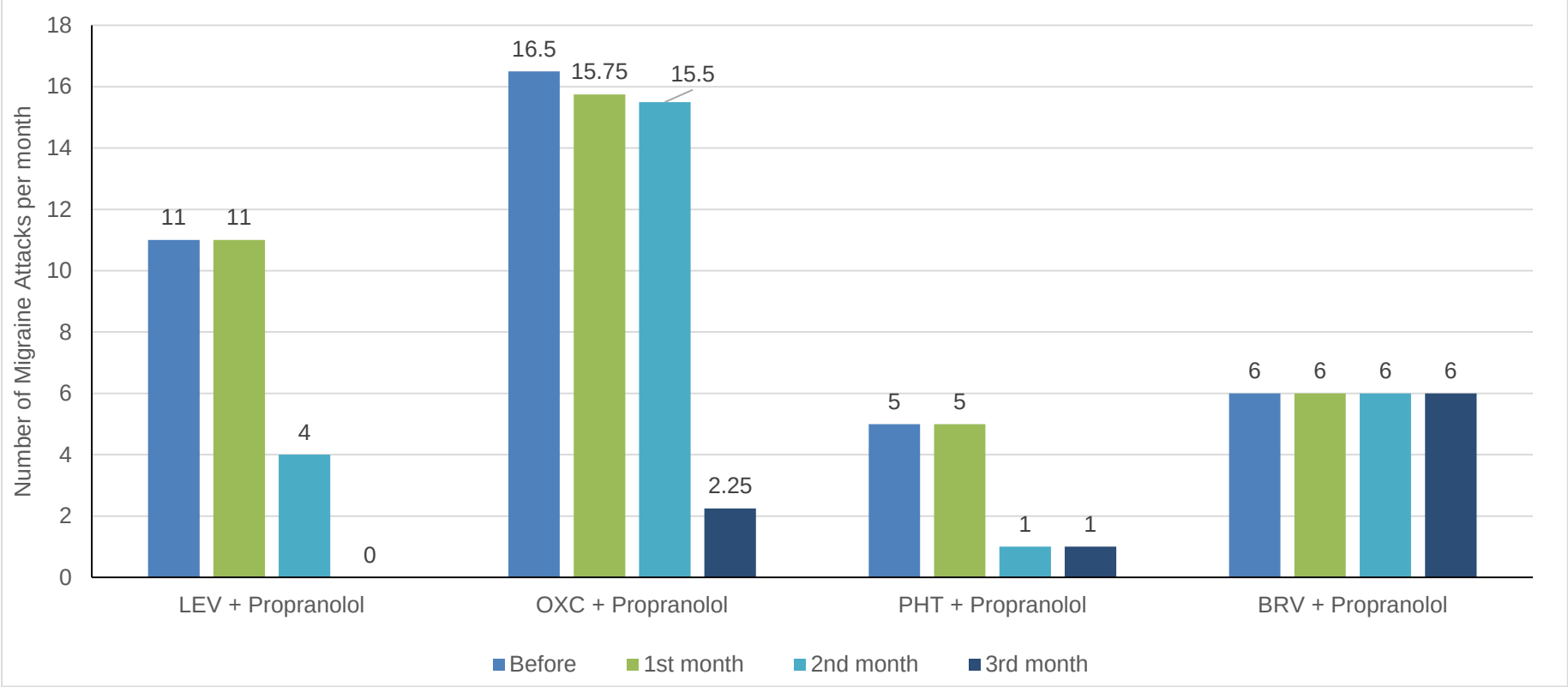


Figure 36

AED+ Propranolol used and mean VAS of migraine in patients of focal with secondary generalization (N=5)

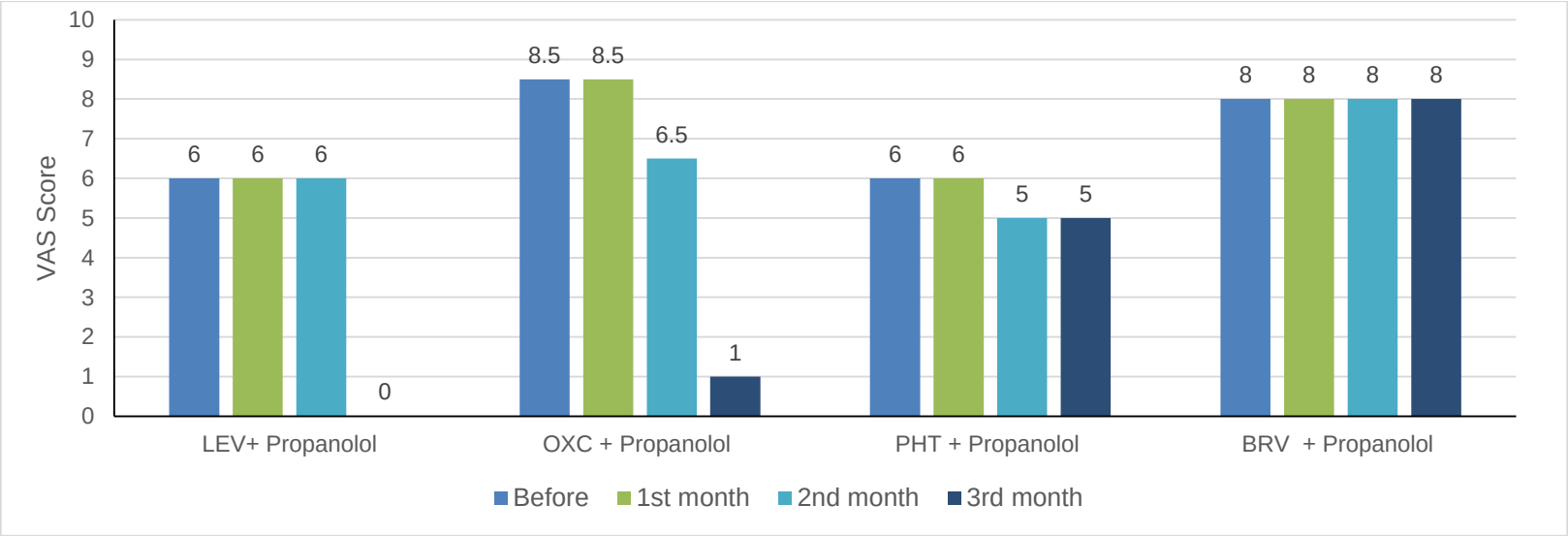


Figure 37

AED+ Propranolol used and mean GAMS of migraine in patients of focal with secondary generalization (N=5)

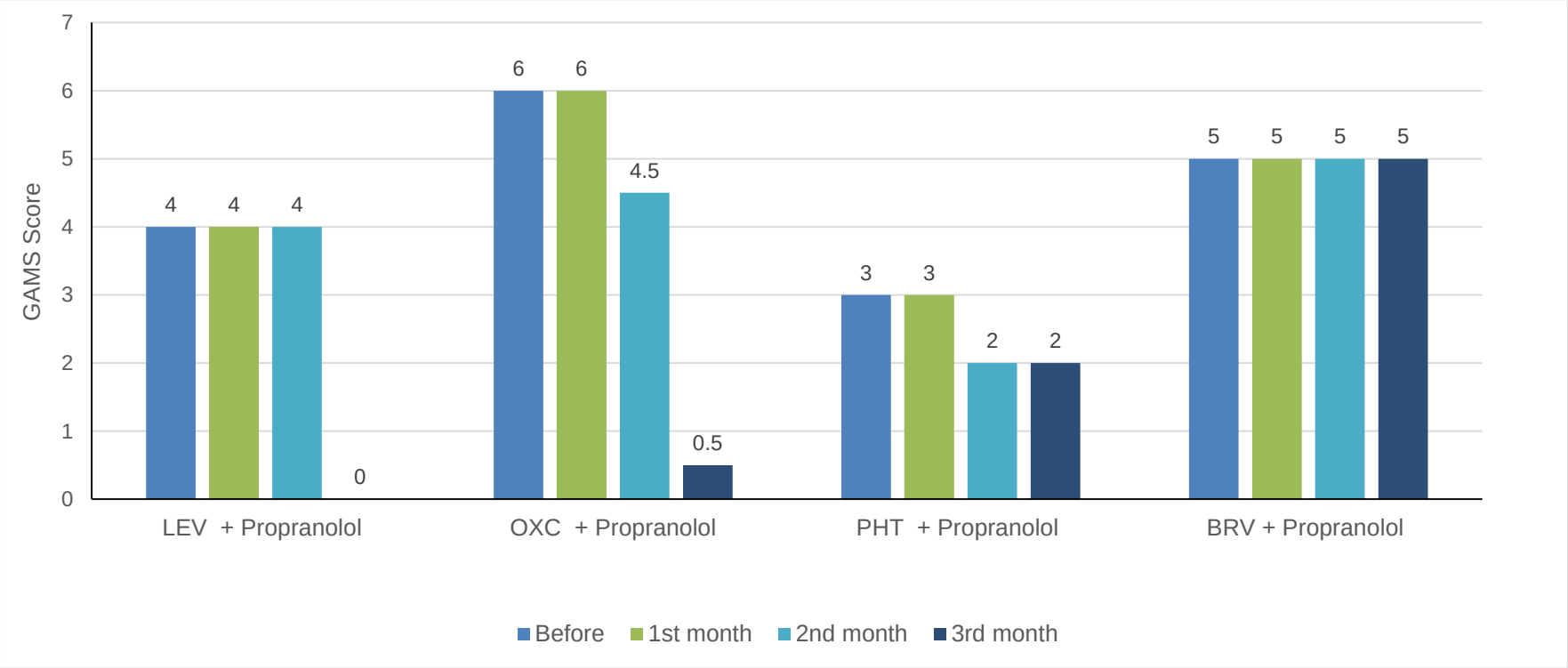


Table 14

Distribution of patients based on AED and dose in patients with migraine and SPS.

Sr No.	AED used	Dose	No of patients
1	LEV	15-20mg/kg	5
		8mg/kg	2
2	OXC	900mg/day	1
Total			8

Figure 38

AED used alone and mean frequency of migraine in patients with simple partial seizures (N=8)

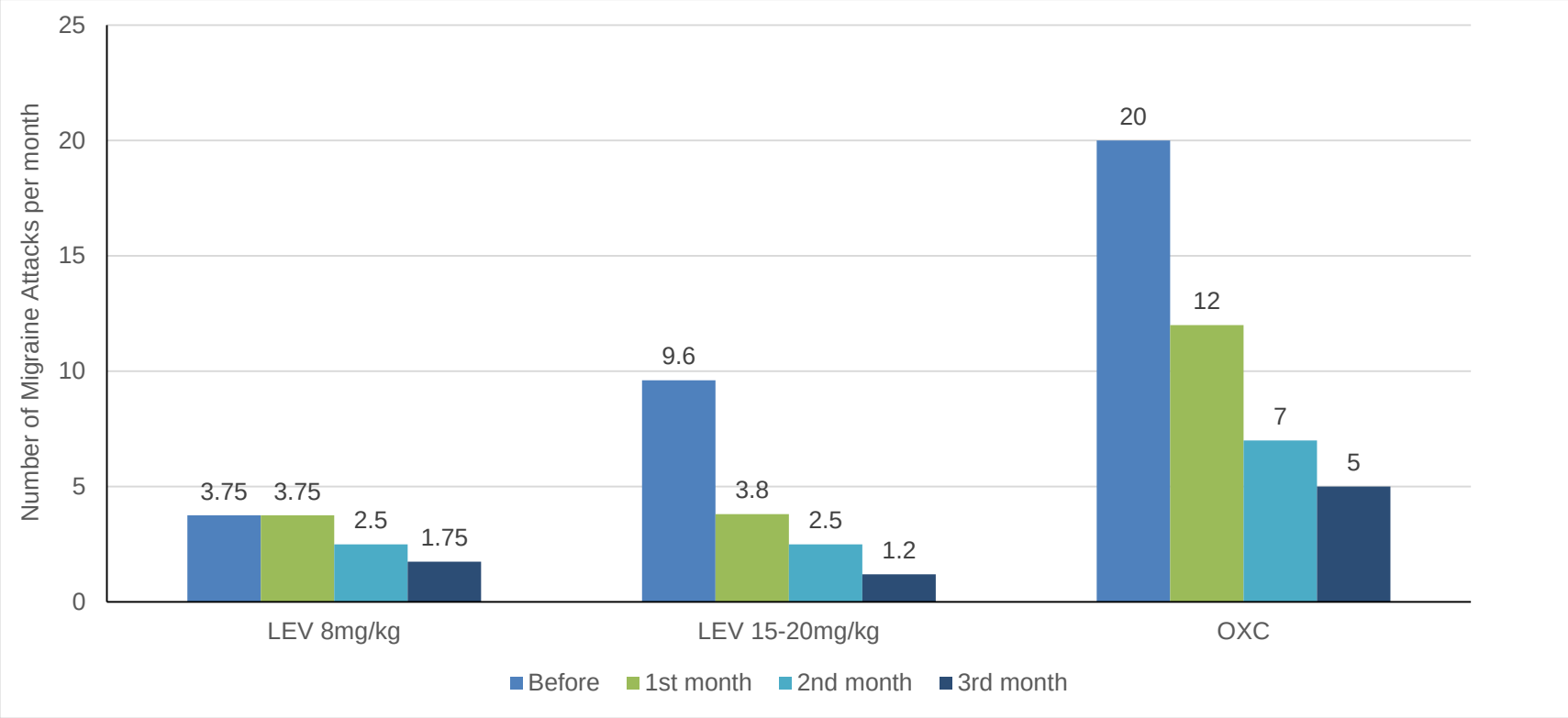


Table 15

Mean frequency with LEV 15-20mg/kg (SPS)

Groups	Mean ± SD
Before	9.6 ± 6.3
1st month	3.8 ± 0.9
2nd month	2.5 ± 1.2
3rd month	1.2 ± 0.9

Groups		Mean Difference	Std. Error	Significance
Before	1st month	5.800	2.411	0.074
	2nd month	7.100	2.657	0.056
	3rd month	8.400*	2.731	0.037
1st month	Before	-5.800	2.411	0.074
	2nd month	1.300	0.539	0.073
	3rd month	2.600*	0.485	0.006
2nd month	Before	-7.100	2.657	0.056
	1st month	-1.300	0.539	0.073
	3rd month	1.300*	0.200	0.003
3rd month	Before	-8.400*	2.731	0.037
	1st month	-2.600*	0.485	0.006
	2nd month	-1.300*	0.200	0.003

Figure 39

AED used alone and mean VAS of migraine in patients with simple partial seizures (N=8)

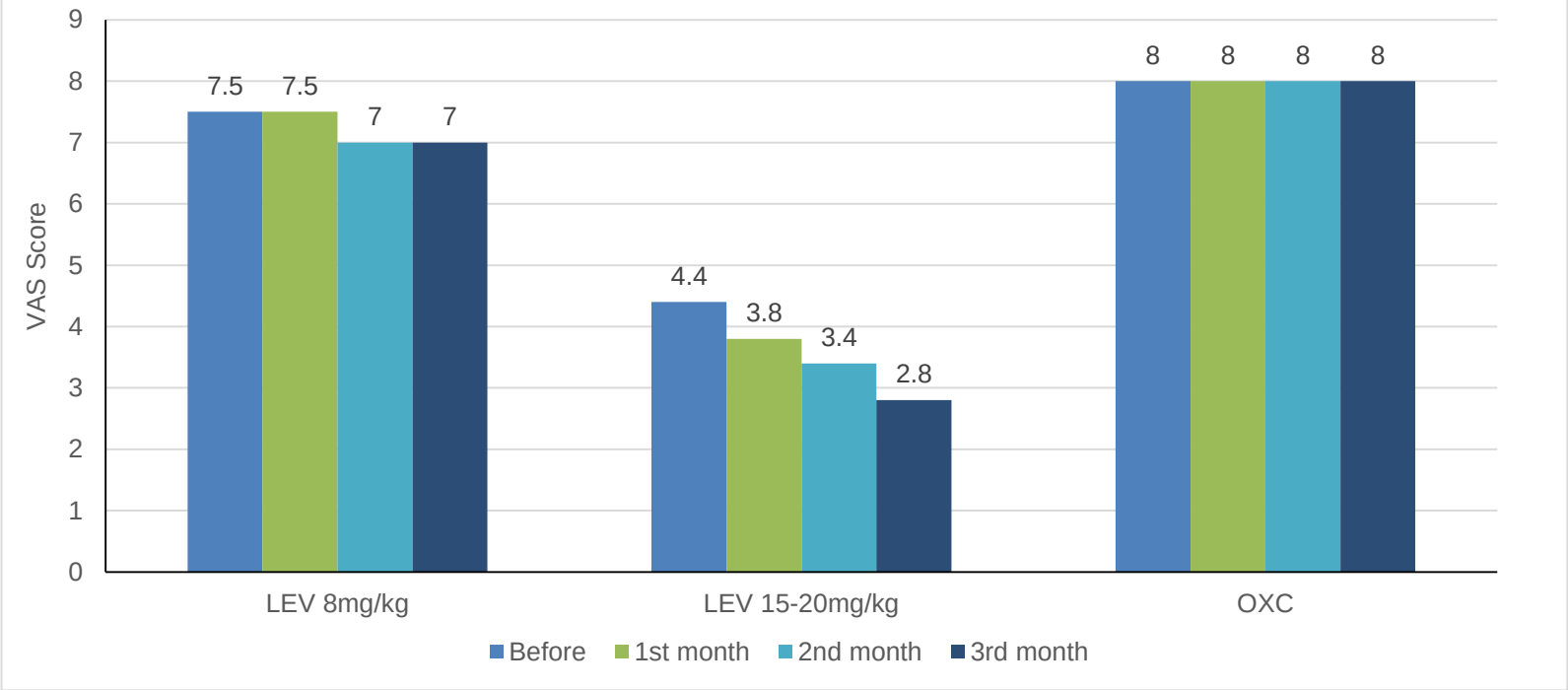


Table 16

Mean VAS score with LEV 15-20mg/kg (SPS)

	Mean ± SD
Before	4.4 ± 3.5
1st month	3.8 ± 2.3
2nd month	3.4 ± 2.6
3rd month	2.8 ± 3.0

Groups		**Mean Difference**	**Std. Error**	**Significance**
Before	1st month	0.600	1.288	0.666
	2nd month	1.000	1.140	0.430
	3rd month	1.600	1.364	0.306
1st month	Before	-0.600	1.288	0.666
	2nd month	0.400	0.245	0.178
	3rd month	1.000*	0.316	0.034
2nd month	Before	-1.000	1.140	0.430
	1st month	-0.400	0.245	0.178
	3rd month	0.600	0.400	0.208
3rd month	Before	-1.600	1.364	0.306
	1st month	-1.000*	0.316	0.034
	2nd month	-0.600	0.400	0.208

Figure 40

AED used alone and mean GAMS of migraine in patients with simple partial seizures (N=8)

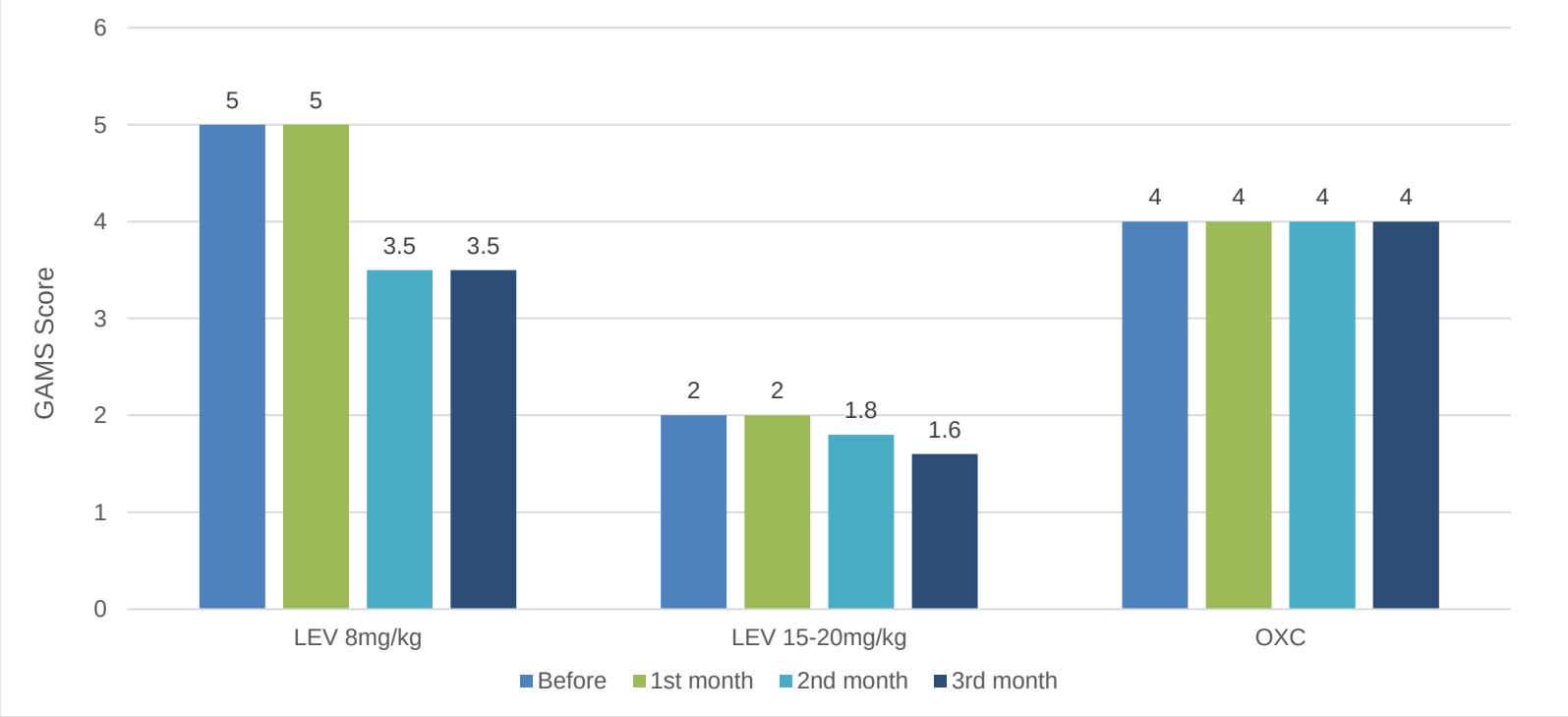


Table 17

Mean GAMS score with LEV 15-20mg/kg (SPS)

Groups	Mean ± SD
Before	2.0 ± 1.7
1st month	2.0 ± 1.7
2nd month	1.8 ± 1.7
3rd month	1.6 ± 1.9

Groups		Mean Difference	Std. Error	Significance
Before	1st month	0.000	0.000	0.0
	2nd month	0.200	0.200	0.374
	3rd month	0.400	0.245	0.178
1st month	Before	0.000	0.000	0.0
	2nd month	0.200	0.200	0.374
	3rd month	0.400	0.245	0.178
2nd month	Before	-0.200	0.200	0.374
	1st month	-0.200	0.200	0.374
	3rd month	0.200	0.200	0.374
3rd month	Before	-0.400	0.245	0.178
	1st month	-0.400	0.245	0.178
	2nd month	-0.200	0.200	0.374

Figure 41

AED used alone and mean frequency of migraine in patients with Myoclonic seizures (N=2)

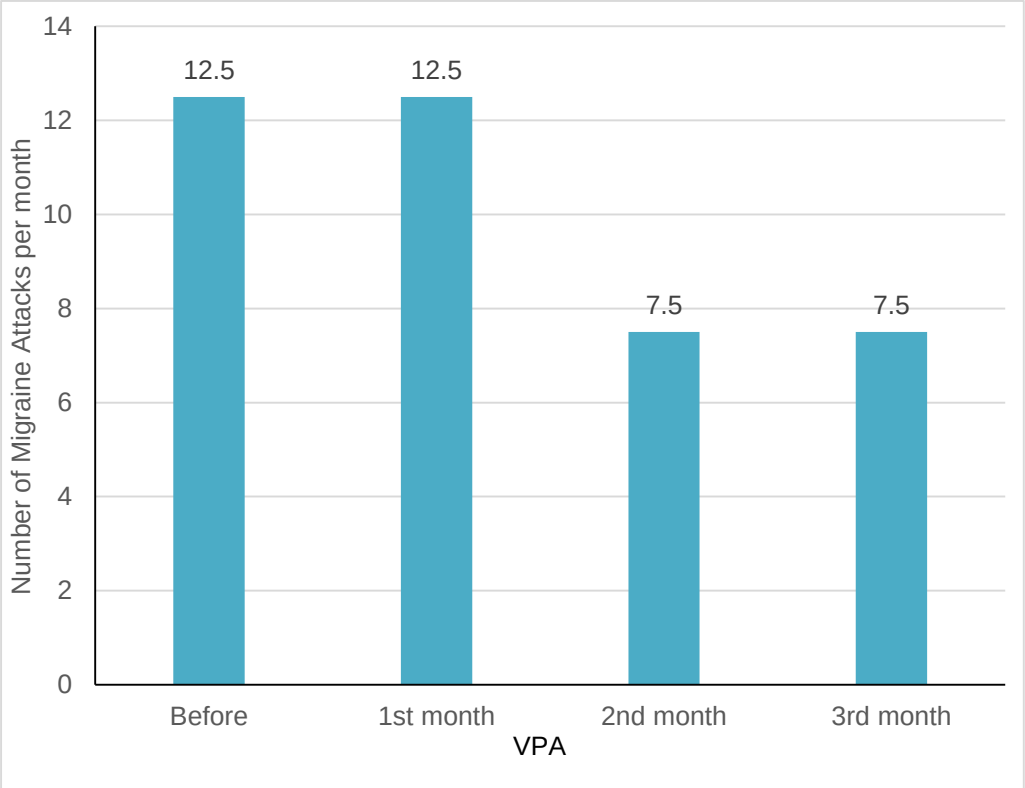


Figure 42

AED used alone and mean VAS of migraine in patients with Myoclonic seizures (N=2)

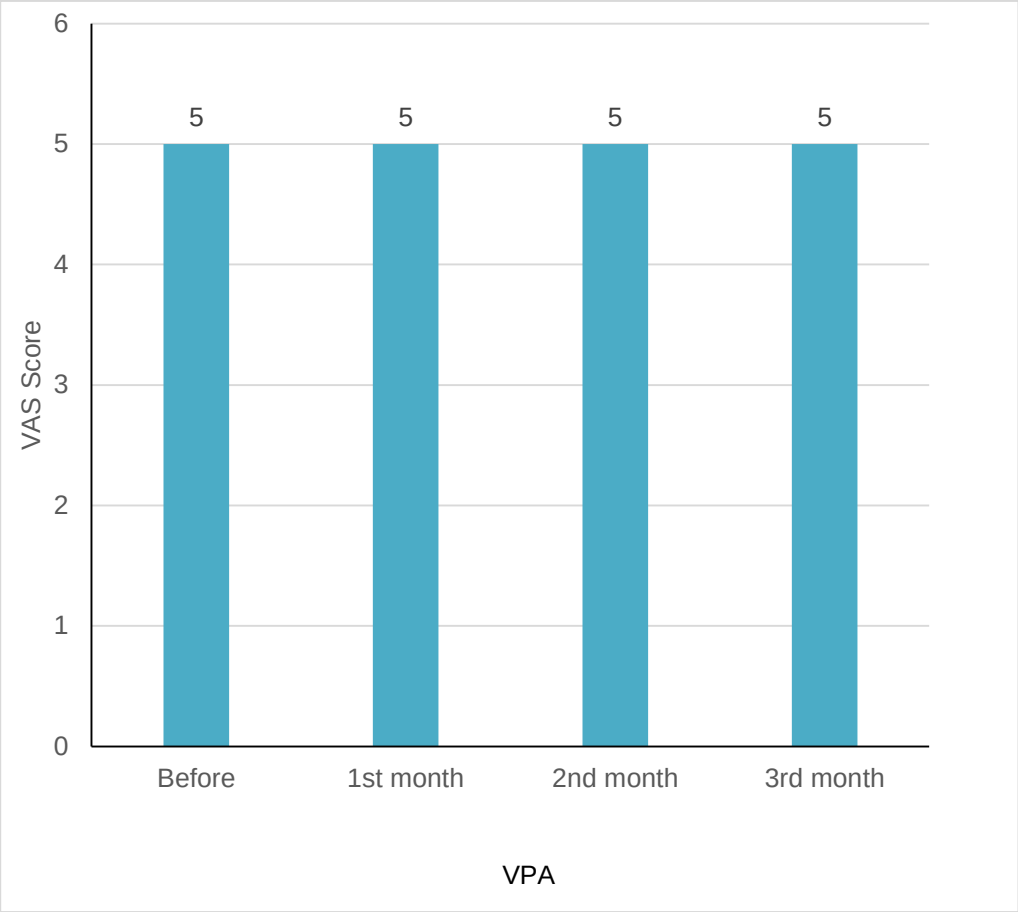


Figure 43

AED used alone and mean GAMS of migraine in patients with Myoclonic seizures (N=2)

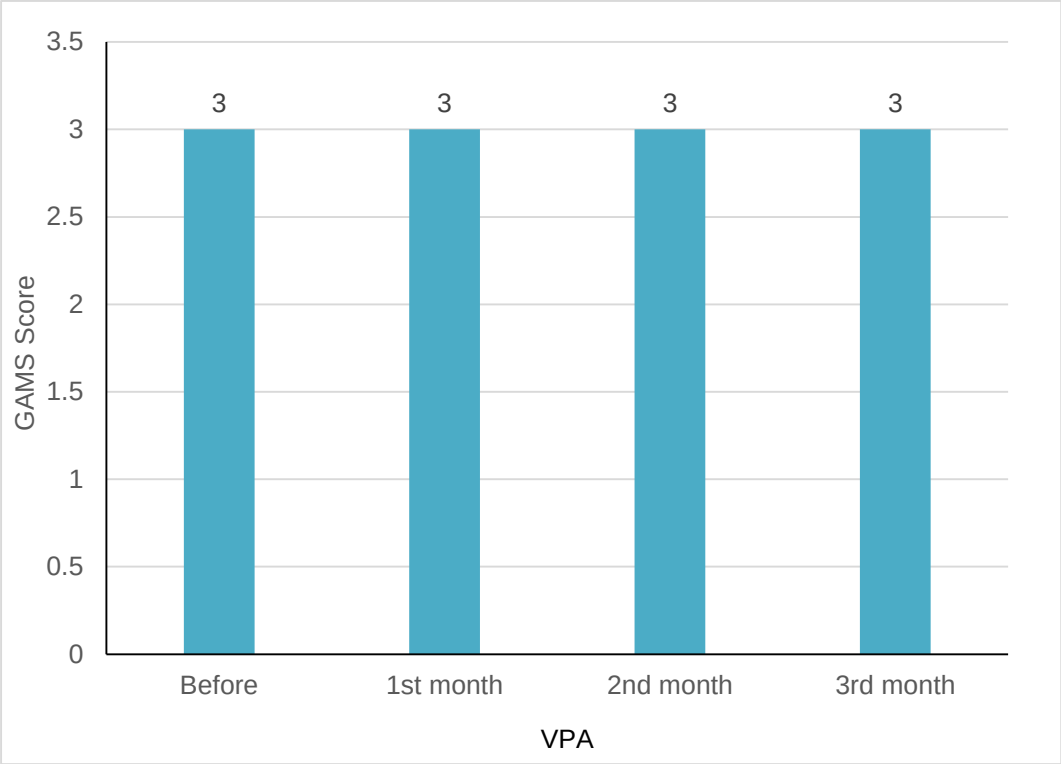


Table 18

Distribution of patients based on AED + Propranolol and dose in patients with migraine and Myoclonic seizures

Sr No.	AED + Propranolol	No of patients
1	TPA 250mg/day + Propranolol 20mg	2
2	LEV 15mg/kg + Propranolol 10mg	1
Total		3

Figure 44

AED + Propranolol used and mean frequency of migraine in patients with Myoclonic seizures (N=3)

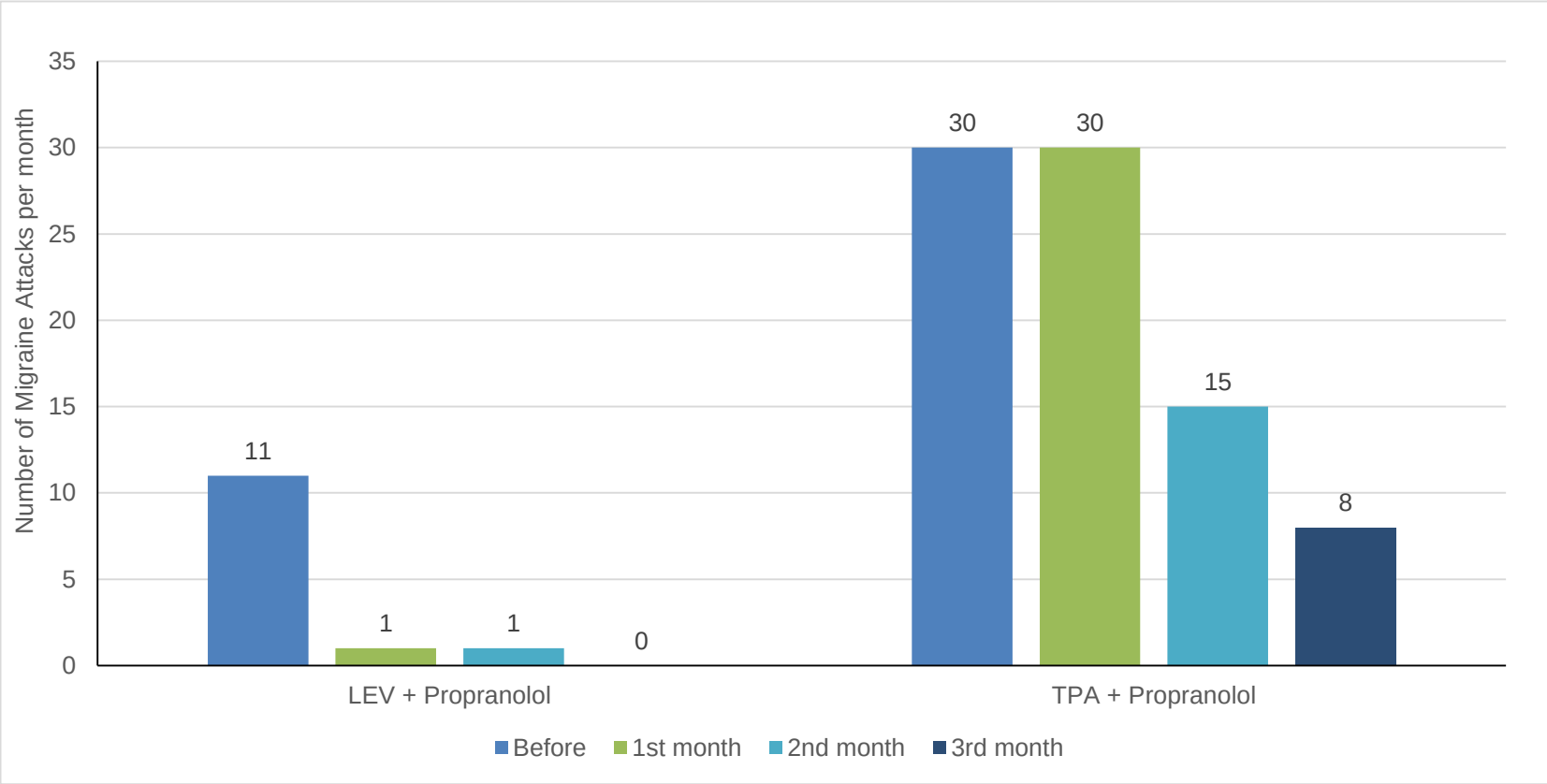


Figure 45

AED+ Propranolol used and mean VAS of migraine in patients with Myoclonic seizures (N=3)

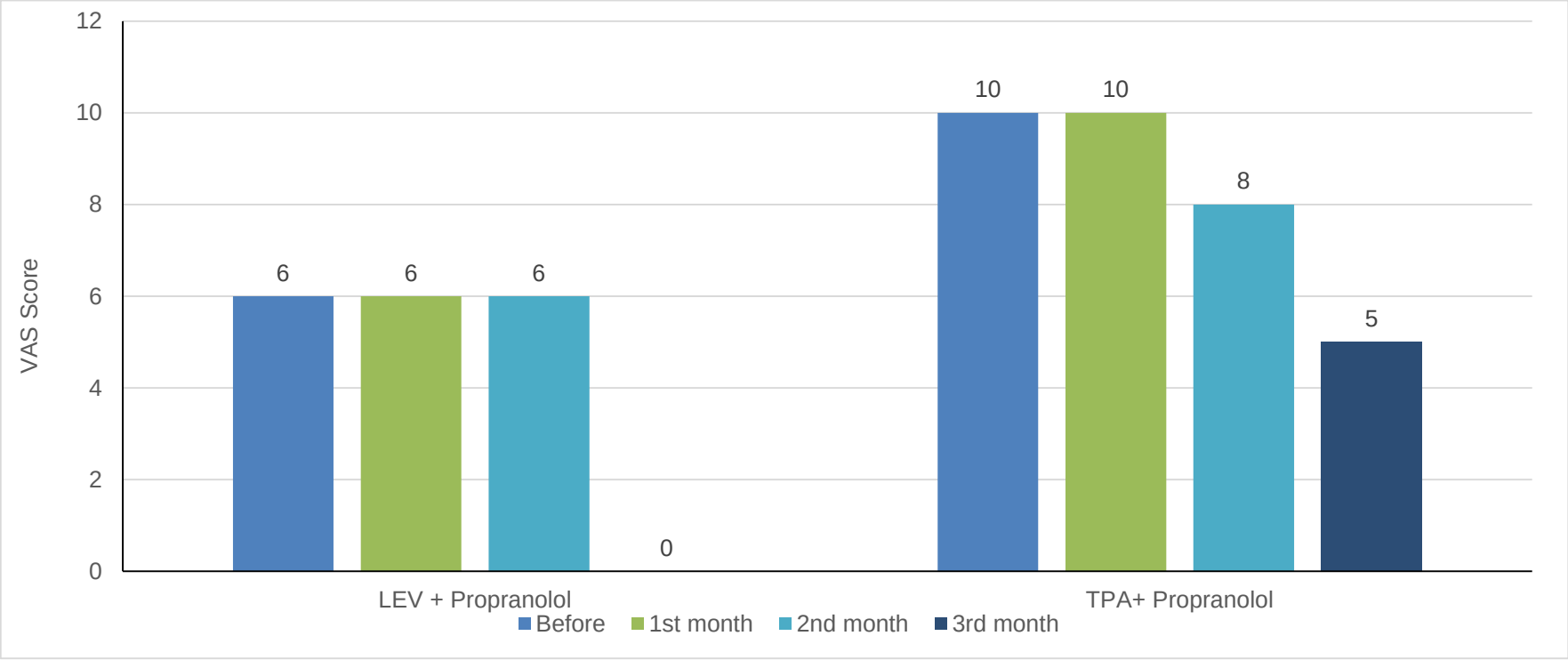


Figure 46

AED+ Propranolol used and mean GAMS of migraine in patients with Myoclonic seizures (N=3)

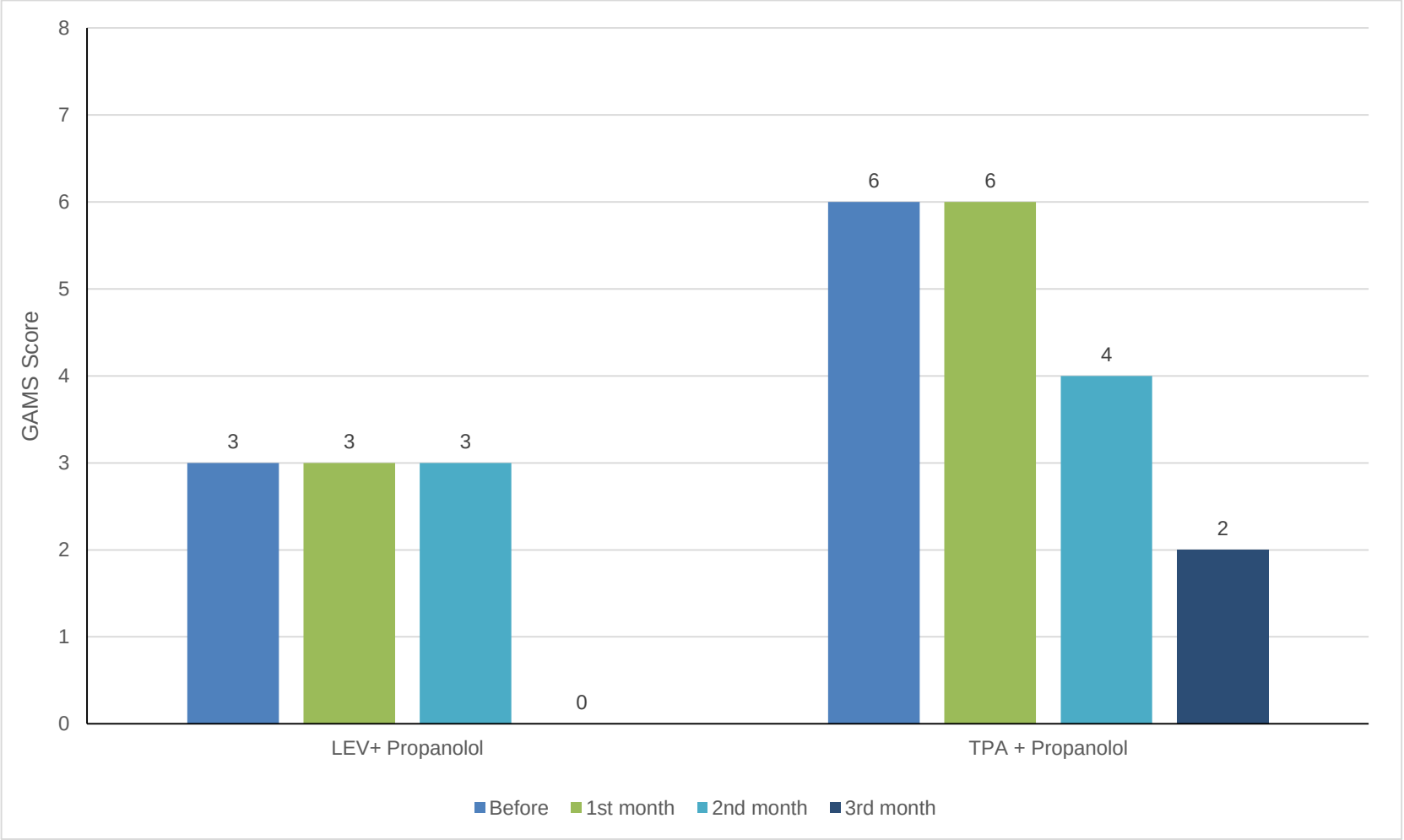
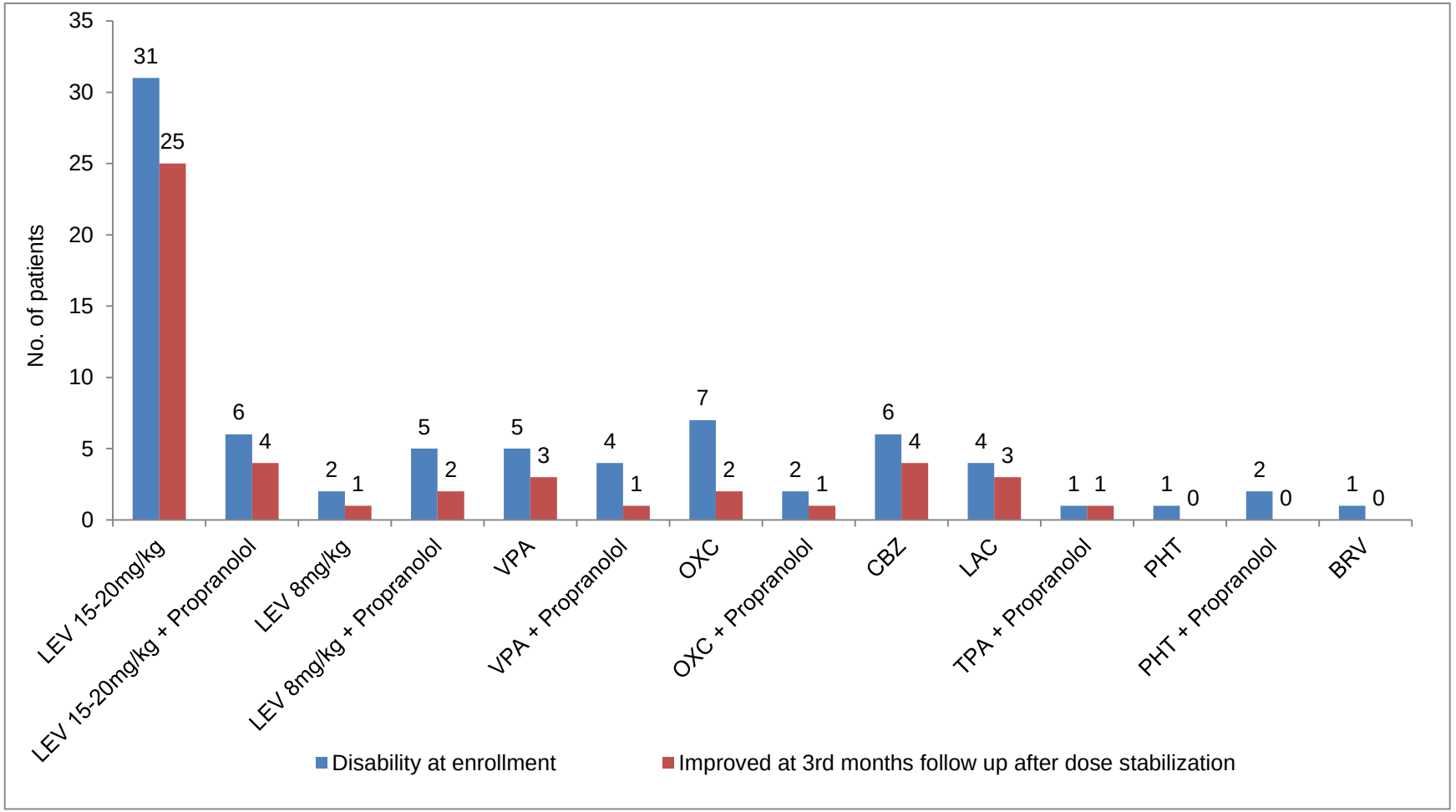


Figure 47

Distribution of Patients with migraine related disability



DISCUSSION

Incidence of headache in general population is 5%- 10%, while it is 8%-23% in patients with epilepsy. Similarly, symptoms of epilepsy in general population are 0.5%- 1%, but in migraine patients it can be up to 5.9% [9]. There is a new term Migralepsy, with only a few cases described in literature because it has been observed that there is some overlap of symptoms between epilepsy and migraine [8,9]. Migraine is mostly characterized by recurrent attacks of headache mainly unilateral or can be bilateral, accompanied by various symptoms such as photophobia, phonophobia, nausea and vomiting. [1]

Both epilepsy and migraine are chronic central nervous system disorders manifesting as episodic or recurrent neurological dysfunction which returns to symptom free baseline status between attacks. Both can have the same precipitating factors such as stress, lack of sleep, exposure to bright light and can be preceded by transient aura and often have genetic involvement or family history. This overlap in clinical manifestations might indicate pathophysiological overlap. Both are acknowledged as originating from electrical disturbances in the brain. In Migraine there is initial increase in neuronal activity which leads to cortical spreading depression and aura. In epilepsy, neuronal activity recruits larger population of neurons which fire in a rhythmic manner.[9]

Because of this overlap in pathophysiology and clinical symptomatology, many AEDs have been approved to be used prophylactically in patients with migraine. Sodium valproate, topiramate & gabapentin are included in the list of drugs approved for prophylaxis of migraine by FDA. [21] Apart from the above-mentioned AEDs many other AEDs like LEV, ZNS, LAC, CBZ also have proven efficacy in migraine. [5]

The treatment of migraine can be either abortive or prophylactic, abortive treatment gives relief from symptoms of acute attack of migraine, while aim of prophylactic treatment is to reduce the frequency as well as severity of headache over the time. Prophylaxis of migraine can reduce

the burden of disease, prevent overuse of analgesics and help in leading normal disability free life. There are various drugs which have been approved to be used prophylactically in patients with migraine, AEDs are one of them. Many AEDs have shown efficacy in migraine but the clinical data is limited. [21]

The present study has been conducted to evaluate the effects of AEDs on frequency, severity and migraine related disability due to migraine, in patients having epilepsy along with migraine. The patients attending the neurology and epilepsy clinic in Dayanand Medical Collage and Hospital, who were suffering from new onset epilepsy and migraine, were recruited. They were started on monotherapy of AED and follow up for 3 months was done after achieving the stable dose of AED in 3 months. The study comprised of 102 clinically diagnosed patients of epilepsy and migraine. The patients were further categorized according to seizure semiology i.e. generalized tonic clonic seizures, myoclonic seizures, simple partial seizures, complex partial seizures and focal with secondary generalization.

In this study it was found that most of the patients belongs to the age group of 21-30 years (N=41, 40.1%) followed by 31-40 years (N= 24, 23.5%). Our result was in conformity with some of the studies which showed the similar data, i.e., the majority of the patients, suffering from migraine fall in age group of 21-40 years. *Hering et al* conducted a double blind placebo-based study on the prophylactic use of sodium valproate in migraine, there were total 29 patients among which majority of the patients fall in the age group of 18- 40 years [37] In our study, there were 56.5% male (N= 58) and 43.1% female (N=44) patients. In various other studies, it has been seen females are more prone to migraine compared to males. In the above mentioned study conducted by *Hering et al,* out of 29 patients, 23 were females and 6 were males [37] Similarly another triple blind, placebo controlled crossover study conducted by *Jenson R* on 34 patients, there were 29 females and 5 men. [38] In our study we recorded many triggering factors for migraine, some of the patients were having more than one triggering factors. In our study

participants, stress (46%) was the most common among all followed by sunlight exposure (37%), travelling (26%), exposure to loud sound (18%), cold (10%). 9% of the patients complained of having migraine attack on doing physical activity, 9% percent due to lack of sleep and 8% due to skipping meals. This was in concordance with the study done on pathophysiology of migraine by *Goadsby et al* [39] who reported similar trigger factors in their study for causing the attack like skipping meals, sleep disturbances, stress, and exposure to sunlight. The pathophysiological role of these factors in causing migraine attack has been explained. [39]

In our study 52.9% (27) patients with GTCS, 60% (3) with myoclonic seizures, 53.8% (7) with focal seizure, 81.25% (13) CPS, 50% (4) SPS and 22.2% (2) of focal with secondary generalization patients, suffered from migraine without aura(56/102) and rest with aura (46/102).

In our study, 51 patients were of GTCS and among them 18 patients were prescribed VPA 20-25 mg/ kg, with mean frequency of 9.42 ± 8.66 migraine attacks per month at the start of treatment, 5.75 ± 7.05 at 1st month follow up, 3.97 ± 6.96 at 2nd month follow up and 3.08 ± 7.07 at 3rd month follow up after dose stabilization. There was significant difference in mean frequency of headache attacks per month (P=0.056) using repeated ANOVA followed by Tukey's test. However, the difference in mean frequency before starting the treatment and 2nd and 3rd month follow up after dose stabilization was statistically significant (P=0.006, P=0.003 respectively). Difference in mean frequency from 1st to 2nd and 3rd month of follow up after dose stabilization was also highly significant (P=0.001, P=0.005). There was no significant difference in mean frequency between 2nd and 3rd month after dose stabilization of follow up (P=0.736).

Similarly, in our study the change in severity of migraine was assessed by using VAS & GAMS score. It was seen that in 18 patients with GTCS prescribed VPA, the mean difference in severity of the migraine attack at the time of enrollment to 2nd (P=0.044) & 3rd (P= 0.001) month follow

up after dose stabilization was statistically significant. The mean difference between the 1st and 3rd month of follow up after dose stabilization was also significant (P= 0.006).

One patient of CPS taking VPA, showed no decrease in mean frequency as well as severity at the end on 3rd month follow up after dose stabilization.

Two patients of myoclonic seizures on VPA showed decrease in mean frequency from 12.5 at baseline to 7.5 at the end of 3rd month follow up after dose stabilization, there was no change in severity at the end of 3rd follow up after dose stabilization.

There were five patients taking VPA 20-25mg/kg with migraine related disability at the enrollment, 3 among them showed improvement at the end of 3rd month follow up after dose stabilization.

Results of our study were in concordance with placebo based, double blind crossover study done with sodium valproate by *Hering et al* on patients with migraine, who studied subjects using crossover design for 8 weeks each in two groups; Sodium valproate 400 mg twice daily v/s placebo. [37] Patients were required to keep a migraine diary to note down the frequency duration and severity of migraine attack along with their use of analgesics to abort the acute attack which was similar to our study. In this study, treatment with sodium valproate significantly reduced frequency of attacks as compared to placebo (P < 0.001) as well as significant reduction in severity of migraine attack (P<0.005). [37] He also reported change in total duration of attacks (P=0.002). There was a strong co relation between the severity of migraine attack and efficacy of sodium valproate. [37] This showed that sodium valproate is very effective medication for prophylaxis of migraine in terms of reducing its frequency as well as severity.

There were four patients who were put on prophylactic treatment (propranolol 10mg/day) along with VPA; there was decrease in mean frequency from 15.5 ± 11.23 at baseline to 2.5 ± 1.15 at the end of 3rd

month follow up after dose stabilization. There was decrease in VAS score at the end of 3rd month follow up after dose stabilization from 8.75 ± 0.96 (at enrollment) to 6.00 ± 2.31, and GAMS score from 4.75 ± 0.96 at enrollment to 3.25 ± 1.50. 4 patients taking prophylactic treatment along with VPA showed migraine related disability at enrollment, only one patient improved at the end of 3rd month follow up after dose stabilization. No similar study was found in literature which studied add on effect of propranolol with VPA. However propranolol alone has been shown to reduce episodes of headache attacks. A meta analysis was done by *Jeffrey L. Jackson*, on efficacy of beta blockers in prevention of migraine attacks in adults. This study included 108 randomized controlled trials among which 50 were placebo-controlled and 58 were comparative effectiveness trials. Result of his study showed that propranolol reduced episodic migraine headaches by 1.5 headaches per month at 8 weeks when compared to placebo. Propranolol reduces the number of analgesic medications use as well as frequency of migraine headache per month by more than 50%. The study also concluded that propranolol reduces the severity or duration of the attacks. [40]

In our study, patients who were on LEV in the dose of 15-20mg/kg showed significant reduction in mean frequency and severity of migraine attack. Mean frequency of migraine attacks per month in the 15 patients of GTCS group who were taking LEV 15-20mg/kg was 7.7 ± 2.04 attacks per month at enrollment, 4.1 ± 0.8 attacks per month on 1st month follow up after dose stabilization, 2.26 ±0.55 attacks per month on 2nd month follow up (P=0.010) after dose stabilization, 1.3 ± 0.45 attacks per month on 3rd month follow up (P=0.006) after dose stabilization. The results were again analysed by using repeated ANOVA followed by Tukey's test. In addition, the difference in mean frequency from 1st month follow up after dose stabilization to 2nd and 3rd month follow up after dose stabilization also showed significant decrease (P=0.001, P=0.005 respectively). Mean difference in frequency of attacks per month between 2nd & 3rd month follow up after dose stabilization is also significant (P=0.003). Difference in mean VAS & GAMS score in patients of GTCS with LEV (15-20mg/kg) between the baseline (at enrollment)

and at the end of 2nd and 3rd month follow up after dose stabilization showed significant decrease (P=0.004, P=0.0001 respectively). Similarly the difference between 1st month to 2nd & 3rd month of follow up after dose stabilization was significant (P= 0.0029, P=0.001 respectively). In GTCS, LEV 8mg/kg showed no decrease in severity. We had one patient of GTCS on LEV 8 mg/kg, who showed promising results, i.e. decrease in frequency of migraine attacks per month from 30 attacks per month at baseline (at enrollment) to 12 attacks per month at the end of 3rd month follow-up after dose stabilization.

In our study there were eight patients with SPS, among them five were on LEV 15- 20 mg/kg. Mean frequency of migraine attacks per month of these five patients who were on LEV 15-20mg/kg was 9.6 ± 6.3 at enrollment, 3.8 ± 0.9 attacks per month on 1st month follow up after dose stabilization, 2.5 ± 1.2 attacks per month on 2nd month follow up after dose stabilization and 1.2 ± 0.9 attacks per month on 3rd month follow up after dose stabilization. After applying repeated ANOVA followed by Tukey's test, it was seen that difference in mean frequency from baseline (at enrollment) to 1st and 2nd month follow up after dose stabilization was not significant but the difference in mean frequency from baseline (at enrollment) to 3rd month follow-up after dose stabilization was statistically significant (P=0.037). Similarly the difference between the 1st and 3rd month follow up after dose stabilization and 2nd and 3rd month of follow up after dose stabilization was significant (P=0.006, P=0.003 respectively). In SPS, with LEV 15-20mg/kg difference in mean VAS score between 1st and 3rd month of follow up after dose stabilization was 1.00 ± 0.316 which was significant (P=0.034). There was no significant decrease in GAMS score. With LEV 8mg/kg there was only slight decrease in severity i.e. from 7.5 at enrollment to 7 (VAS score) and 5 at enrollment to 3.5 (GAMS score) at the end of 2nd and 3rd month follow up after dose stabilization. There were two patients who were prescribed LEV 8mg/ kg, not much decrease in mean frequency and severity has been seen in them.

In CPS group, 4 patients on LEV 15-20mg/kg had decrease in mean frequency from 10.12 ± 13.33 at enrollment to 3.13 ± 3.88 attacks per month at the end of 3rd month follow up after dose stabilization. VAS reduced from 6.75 ± 2.50 to 2.75 ± 3.40 and GAMS from 4.25 ± 2.06 to 4.00 ± 1.50 at the end of 3rd month follow up after dose stabilization. One patient was on LEV 8mg/kg who showed maximum decrease in frequency i.e. from 27.50 at enrollment to 7.50 at 2nd month follow up and to 2.5 by the end of 3rd month after dose stabilization, VAS decreased from 8 to 3 and GAMS from 4 to 2.

In focal seizure, with LEV 15-20mg/kg mean frequency decreased from 6.00 ± 7.72 at enrollment to 1.50 ± 2.12 attacks per month and VAS reduced from 5 to 4 and GAMS from 3 to 2.5 at the end of 3rd month follow up after dose stabilization. Maximum decrease in mean frequency was seen with LEV 8mg/kg i.e. from 14.50 ± 18.38 at enrollment to 2.00 ± 0.71 attacks per month at end of 3rd month follow up after dose stabilization and mean VAS decreased from 7.5 to 5 and GAMS from 4 to 3. In Focal with secondary generalization there were 4 patients who were on LEV 20mg/kg, they showed decrease in mean frequency from 2.50 ± 2.50 at enrollment to 1.80 ± 1.44 attacks per month at the end of 3rd month follow up after dose stabilization. There was not much change in severity seen at the end of 3rd month follow up after dose stabilization.

Among 77 patients with migraine related disability, 31 were on LEV 15-20mg/kg, by the end of 3rd month follow up after dose stabilization 25 among them improved. Two patients of LEV 8mg/kg had migraine related migraine related disability at the enrollment, one showed improvement at the end of 3rd month follow up after dose stabilization. There were 5 patients who were taking LEV 8mg/kg along with propranolol 10mg/day had migraine related disability at the enrollment, 2 showed improvement at the end of 3rd month follow up.

There were few patients who were put on prophylactic treatment (propranolol) along with LEV. In GTCS, there were 3 patients who were

taking LEV 15-20mg/kg + propranolol 10mg/day, they showed decrease in mean frequency at the end of 3rd month follow up after dose stabilization from 13.5 ± 14.8 (at enrollment) to 6.5 ± 9.6 per month. Decrease in mean VAS score at the end of 3rd month follow up after dose stabilization was from 9.00 ± 1.00 (at enrollment) to 3.67 ± 3.21, similarly GAMS score decreased from 4.33 ± 1.53 (at enrollment) to 2.33 ± 2.08.

In patients with CPS started on LEV 20mg/kg + propranolol 10mg/day mean frequency decreased from 30 (at enrollment) to 10 attacks per month by end of 3rd month follow up after dose stabilization. There was no decrease in severity with LEV 20mg/kg + propranolol 10mg/day. With LEV 8mg/kg + propranolol 10mg/day mean frequency decreased from 15 (at enrollment) to 4.5 attacks per month by the end of 2nd and 3rd month follow up after dose stabilization. Mean VAS decreased from 15 (at enrollment) to 4.5 and GAMS score decreased from 5 (at enrollment) to 2 by the end of 2nd and 3rd month follow up after dose stabilization.

In patients with focal seizure started on LEV 18mg/kg + propranolol 10mg there was decrease in frequency from 12.5 to no attack at the end on 3rd month follow up after dose stabilization. There was not much decrease in severity. In focal with secondary generalization with LEV 20mg/kg + propranolol 10mg/day mean frequency decreased from 11 at enrollment to no attack per month at the end of 3rd month follow up after dose stabilization.

In patients with myoclonic seizures started on LEV 15mg/kg + propranolol 10mg, there was decrease in frequency from 11 at enrollment to 1 attack per month at the end of 1st and 2nd follow up and no attacks per month at the end on 3rd month follow up after dose stabilization. Among 31 patients on LEV 15-20mg/kg with migraine related disability, six were taking LEV 20mg/kg + propranolol 10mg/day, four among them showed no migraine related disability at the end of 3rd month follow up after dose stabilization.

Our results are comparable with the similar study done by *Verma et al.*[41] in rural medical institute of North India using randomized placebo

controlled study for LEV in migraine prophylaxis. A total of 65 patients were randomized in 1:1 to receive LEV & placebo. LEV was titrated to the maximum dose of 1000 mg/ day. It showed significant reduction in the frequency of attacks per month from 5.13 at baseline to 2.21 in the last 4 weeks. *Verma et al*, also reported decrease in migraine severity from 2.75 to 1.29 when compared to placebo group. [41]

Result of our study was also comparable to a systemic review and metanalysis which was done by *Po-Hua Yen* on efficacy of LEV in migraine prophylaxis. [42] Four randomized controlled trials using LEV in a therapeutic range of 500-3000mg per day (which translates as 15-20mg/kg) showed that there was 50% reduction in headache frequency in LEV group as compared to placebo. After medication some patients were completely free from migraine attacks. *Yen et al*. [42], also assessed change in severity of migraine by using VAS. The baseline VAS score was 2.56 ± 0.44 which was reduced to 1.48 ± 0.45 and 1.32 ± 0.46 at the end of 3rd and 6th month respectively. This proves that LEV in the therapeutic range shows promising results in decreasing migraine frequency as well as severity[41] No study is available which demonstrates add on effect of propranolol with LEV. However, propranolol alone showed significant efficacy in reducing the frequency as well as severity of migraine attacks [40]

In our study patients on CBZ 20 mg/kg also showed decrease in Migraine attacks and severity. In GTCS they showed decrease in mean frequency from 13.5 ± 8.26 attacks per month at baseline (at enrollment) to 7.8 ± 7.52 attacks per month at the end of 3rd month follow up after dose stabilization. Similarly, the mean VAS score was reduced from 8.3 ± 1.53 at baseline (at enrollment) to 5.00 ± 4.36 at the end of 3rd month follow up after dose stabilization and mean GAMS score was reduced from 4.7 ± 2.08 at baseline (at enrollment) to 2.3 ± 2.08 at the end of 3rd month follow up after dose stabilization.

In patients with CPS started on CBZ 20mg/kg mean frequency decreased from 11.75 ± 10.25 at enrollment to 7.50 ± 10.61 attacks per month at the end of 3rd month follow up after dose stabilization. VAS and

GAMS score reduced from 8 to 4 & 4.5 to 2 respectively. In focal seizure, mean frequency decreased from 20 at enrollment to 10 attacks per month at 3rd month follow up after dose stabilization. The result was comparable to the placebo based double blind crossover study done by *Rompel*, which showed highly significant reduction in frequency of migraine attacks with CBZ compared to placebo. [43]

Patients who were started on OXC 900-1200 mg/day in our study also showed promising results. In GTCS, there was decrease in mean frequency from 9.5 ± 11.31 at baseline (enrollment) to 4.8 ± 6.72 at the end of 3rd month follow- up after dose stabilization, decrease in mean VAS score was from 5.00 ± 2.83 at baseline (enrollment) to 2.00 ± 2.83 at the end of 3rd month follow- up after dose stabilization and GAMS score was reduced from 1.50 ± 0.71 to 1.00 ± 1.41 at the end of 3rd month follow- up after dose stabilization.

In patients with SPS started on OXC 900-1200 mg/day there was decrease in frequency from 20 attacks per month at baseline (enrollment) to 5.5 at the end of 3rd month follow up after dose stabilization; there was no decrease in severity. In focal seizure, decrease in mean frequency was from 3.00 ± 2.12 at baseline to 1.25 ± 0.35 and there was slight decrease in mean severity at the end of 3rd month follow-up after dose stabilization.

In patients with CPS started on OXC 900-1200 mg/day there was decrease in mean frequency from 7.63 ± 8.37 at baseline (enrollment) to 5.75 ± 6.25 at the end of 3rd month follow up after dose stabilization and no decrease in severity. All the patients who were on OXC with different seizures semiology showed decrease in mean frequency at the end of 3rd month follow up after dose stabilization but there was no significant decrease in severity. Only 2 patients showed improvement at the end of 3rd month follow after dose stabilization out of 7 who showed migraine related disability at the time of enrollment.

The result of my study was in contrast to a double blind, randomized, placebo-controlled study done by Silberstein S et all on OXC in migraine

which concluded that OXC was safe and well tolerated by the patients but did not show efficacy in decreasing the frequency of migraine attacks.[44] However, our study has shown a definite decrease in terms of frequency and severity of migraine (VAS and GAMS).

There was one patient with CPS who was put on prophylactic treatment with propranolol along with OXC. There was decrease in frequency from 12 attacks per month at baseline to 3 attacks per month at the end of 3rd month follow up after dose stabilization but there was no change in severity of attacks.

Patients on LAC 350 mg/day also showed promising results. In those with GTCS, there was a decrease in mean frequency of migraine attacks per month from 12.5 at baseline (at enrollment) to no attack at the end of 1st, 2nd and 3rd month follow-up after dose stabilization.

In patients with focal seizure on LAC 350mg/day, mean frequency decreased from 18.25 ± 16.62 to 10.00 ± 14.14 at the end of 3rd month follow up after dose stabilization. Similarly, severity was also decreased from 4.00 ± 0.00 to 1.5 ± 2.12.

Patients with Complex partial seizure started on LAC 350 mg/day also showed decrease in mean frequency and severity on 3rd month follow up after dose stabilization. There were 4 patients on LAC 350mg/day with migraine related disability at enrollment, 3 among them showed improvement at the end of 3rd month follow up after dose stabilization.

Our study is comparable to a similar study done by *Yaun et al* [45] to assess the effect of LAC on chronic migraine. It was a single centre retrospective analysis done on six patients, results of the study showed that there was a mean reduction by 9.83 days, and pain levels associated with headaches by 1.17 following administration of lacosamide. It also showed decrease in migraine disability Assessment (MIDAS) scores by 36.17. [45]

One patient with GTCS in our study was prescribed prophylactic treatment along with LAC. With LAC 350mg/day + Propranolol 10mg/day

decrease in mean frequency at the end of 2nd and 3rd month follow up after dose stabilization from 20 (at enrollment) to 4.5 attacks per month was seen. There was no similar study in the literature.

We had two patients with myoclonic seizures who were started on TPA 250 mg/day along with Propranolol 20 mg, it was seen that there was decrease in mean frequency of migraine attacks per month from 30 attacks to 8 attacks per month at the end of 3rd month follow up after dose stabilization. *Ashtari et al*, [46] conducted a double-blind randomized trial to compare efficacy of low dose TPM v/s Propranolol in migraine prophylaxis. This study was done on 62 patients and follow up was done for 8 weeks, patients were randomly divided into 2 groups, one treated with TPM 50 mg/ day and other with propranolol 80 mg/ day. The result showed that with TPM there was reduction in mean frequency of migraine attacks per month from 6.07±1.89 to 1.83 ± 1.39 attacks per month and with propranolol mean headache frequency declined from 5.83±1.98 to 2.2±1.67 attacks per month. [46]

Both the drugs in our study were used together and it was found that there was no change in severity of the migraine attacks at the end of 1st, 2nd & 3rd month follow up after dose stabilization which was assessed by using VAS and GAMS scale. This was in contrast to above mentioned study done by *Ashtari et al*[46] which concluded that there was decrease in headache intensity from 7.1±1.45 to 3.67±2.1 at the end of follow-up with TPM 50mg /day, this was also assessed by using VAS similar to our study, they also concluded significant reduction in headache duration from 16.37±7.26 to 6.23±5.22 hrs (P<0.001). With propranolol the intensity decreased from 6.43±1.6 to 4.13±1.94 and duration of headache decreased from 15.10±6.84 to 7.27±6.46 hrs. [46]The study concluded that both the drugs significantly reduce the migraine, frequency, intensity and duration but in comparison to propranolol, low dose TPM showed better results. A true comparison of this study cannot be done with the present study as the dose of TPA used in our study is much higher i.e. 250 mg/day and our patient was taking both drugs (TPM & Propranolol).

Our results were comparable with a randomized controlled trial done on TPM for the prevention and treatment of migraine by *Brandes* et al.[47] In his study, primary efficacy measure was a comparison of the reduction in mean 28-day migraine frequency from the baseline between topiramate and placebo groups. In the placebo group, the mean frequency of migraine attacks per month decreased from 5.6 to 4.5 and larger decreases were observed with TPM. With TPM in dose of 50 mg/day it reduced from 5.4 to 4.1; with TPM 100 mg/day, mean migraine frequency reduced from 5.8 to 3.5 attacks per month and with TPM 200 mg/day, migraine attacks reduced from 5.1 to 3.0 attacks per month. The decrease in migraine attacks per month was only significant with TPM 100 and 200 mg/day. But in contrast, decrease in migraine frequency with TPM was not associated with a reduction in number of migraine days and use of acute rescue medication.[47]

As mentioned earlier no study is available in literature which demonstrates the add on effect of propranolol. However a metanalysis done by *Jeffrey L. Jackson*, proves the efficacy of beta blockers in prevention of migraine attacks in adults. [42]

In our study, there was only one patient with GTCS who was started on PHT 400 mg/day, showed decease in mean frequency from 5 to 1 attack per month at the end of 3rd month follow up after dose stabilization. There was no decrease in severity of migraine. This patient had migraine related disability at the enrollment and showed no improvement in migraine related disability at the end of 3rd month follow up after dose stabilization.

Our results are similar to the study done by *Millichap*, who explored the role of phenytoin in headache and reported improvement in 77% of paediatric patients with migraine, although no exact decrease in number of attacks were given [48]

Patients on prophylactic treatment along with PHT 400mg/kg, showed decrease in frequency without change in severity. In GTCS with PHT 400 mg/kg + Propranolol 10 mg/kg, there was decrease in mean

frequency of migraine headaches from 30 to 7.5 attacks per month at the end of 3rd month follow up. There was not much decrease in severity at the end of 3rd month follow up after dose stabilization.

In the patients with focal seizure, decrease in frequency was from 9 attacks per month to no attack at the end of 2nd and 3rd month follow up after dose stabilization. There was no decrease in severity of pain.

In focal with secondary generalization, there was decrease in frequency from 5.5 to 1.5 at the end of 2nd & 3rd month follow-up after dose stabilization without much decrease in severity at the end of 3rd month follow up after dose stabilization.

Two patients on PHT 400mg + propranolol 10mg with migraine related disability at the enrollment, showed no improvement at the end of 3rd month follow up. There was no similar study available in literature.

In present study, there were only two patients who were taking BRV 100 mg/day, one among them was also put on prophylactic treatment (Propranolol 10mg/day). However the patient without prophylactic treatment showed decrease in frequency from 12.5 attacks per month to 2.5 attacks per month at the end of 1st month follow up after dose stabilization which was maintained till the end of 3rd month post dose stabilization and mean decrease in VAS score from 9 to 7 and GAMS score from 5 to 4 at the end of 1st month after dose stabilization which was also maintained till the end of 3rd month follow up after dose stabilization. Patient on prophylactic treatment along with BRV showed no change in frequency and severity of migraine attack. There was 1 patient on BRV 100mg/day with migraine related disability, showed no improvement at the end of 3rd month follow up. There was no similar study found in literature which shows efficacy of BRV in migraine.

Out of total 102, there were 77 patients with migraine related disability. In 38.9% (N=30) of study subjects no improvement was observed and rest 61.1% (N= 47) of patients showed reduction in migraine related disability.

Our study showed that various AEDs are effective in reducing the frequency, severity and migraine related disability. Use of propranolol prophylaxis increase effectiveness of AEDs in patients with migraine. However more focussed studies are needed for drug specific effects in larger population in multicentric setting.

SUMMARY AND CONCLUSION

The present study was conducted to study the effects of various AEDs on migraine in terms of frequency, severity and disability. This study was conducted over a period of one year. A total of hundred and two clinically diagnosed patients of new onset epilepsy with migraine on monotherapy (AED) were recruited and a follow up was done for 3 months after dose stabilization (3 months). Patients were categorized on the basis of seizure semiology, AED used according to the dose and prophylactic treatment taken. The observations and results were tabulated and graphically represented. The summary of observations is as follows:

- In patients of GTCS, maximum decrease in mean frequency of headache attacks at the end of follow up after dose stabilization was achieved with LEV 8mg/kg followed by LAC. In addition LEV 15-20mg/kg and VPA showed significant decrease. BRV, OXC, CBZ, PHT also showed decrease in mean frequency of headaches per month. Earliest and maximum decrease in mean frequency of headache attacks per month was seen with LAC and BRV. In terms of severity statistically significant decrease is seen with VPA and LEV 15-20mg/kg. With prophylactic treatment (propranolol) along with AED, maximum and earliest decrease in mean frequency of headache attacks per month was achieved with PHT followed by LAC.
- In patients with complex partial seizures, maximum decrease in frequency and severity of headache attacks per month was seen with LEV 8mg/kg followed by LEV 15-20mg/kg and CBZ. OXC and VPA showed no decrease in severity. Use of propranolol prophylactically increased efficacy of LEV 20mg/kg in terms of decreasing frequency of migraine attacks but no change in severity was seen.
- In focal seizures maximum decrease in mean frequency of headache attacks per month was seen with LEV 8mg/kg followed

by CBZ and least with OXC. Maximum decrease in severity was seen with LEV 8mg/kg and OXC, least with LEV 15-20mg/kg. With prophylactic treatment (propranolol), both LEV and PHT along show similar results in terms of frequency but PHT shows more decrease in severity as compared to LEV.

- In focal seizures with secondary generalization, there was not much decrease in frequency as well as severity of headache with LEV. With prophylactic treatment along with AED, maximum decrease in mean frequency and severity was seen with OXC + Propranolol. BRV + Propranolol showed no decrease in frequency as well as severity.
- In simple partial seizures, LEV 15-20mg/kg showed significant decrease in frequency of migraine attacks per month and maximum decrease in frequency of headache was seen with OXC.
- In myoclonic seizures, VPA showed decrease in mean frequency but no decrease in severity of headache attacks. With prophylactic treatment, TPA + Propranolol showed great decrease in frequency as well as severity of migraine attacks.
- Out of 102 study subjects,77 patients had migraine related disability at time of enrollment. In 38.9% of study subjects no improvement was observed and rest 61.1% of patients showed reduction in disability. Among all AEDs, LEV in dose of 8mg/kg and 15-20mg/kg showed maximum decrease in disability all types of seizures
- OXC and LAC seems to be promising AED for use in migraine prophylaxis, although there is limited literature available on it till date
- Our study showed that various AEDs are effective in reducing the frequency, severity and disability of migraine attacks. However, more studies on larger population are required.

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S.No	Initials	Age	gender	Residence	Occupation	SE Status Upper	Upper middle	lower middle	Upper lower	lower	Enrollment Date	Age Onset Epi	Age Onset Epi Range 11-20yrs	21-30yrs	31-40yrs	41-50yrs	51-60yrs	Epi Dur Enroll	Semiology	GTCS	Myoclonic	Focal Motor	CPS	SPS	Focal with Sec. Generalization	Freq Sz	Age Onset Mig	Mig Dur Enroll
1	YS	28	M	rural	farmer	No	No	No	No	No	02-01-2020	28	No	Yes	No	No	No	No	6	No	No	No	No	No	Yes	1	28	Yes
2	SM	34	M	urban	Field worker	No	No	Yes	No	No	01-02-2020	34	No	No	Yes	No	No	No	3	No	No	Yes	No	No	No	1	30	Yes
3	A	19	M	urban	Student	No	No	Yes	No	No	03-02-2020	19	Yes	No	No	No	No	No	1	Yes	No	No	No	No	No	1	15	Yes
4	IS	37	M	rural	farmer	No	No	Yes	Yes	No	08-02-2020	36	No	No	Yes	No	No	No	1	Yes	No	No	No	No	No	2	33	Yes
5	D	19	M	urban	labour	No	No	No	No	Yes	05-03-2020	19	Yes	No	No	No	No	No	6	No	No	No	No	No	Yes	2	17	Yes
6	HK	19	F	urban	Student	No	No	Yes	No	No	24-05-2020	15.5	Yes	No	No	No	No	No	1	Yes	No	No	No	No	No	5	18	Yes
7	SA	52	F	urban	housewife	No	No	Yes	No	No	25-05-2020	50	No	No	No	No	Yes	No	5	No	No	No	No	Yes	No	3	30	Yes
8	RK	26	F	rural	housewife	No	No	No	Yes	No	02-06-2020	24	No	Yes	No	No	No	No	2	No	Yes	No	No	No	No	2	26	Yes
9	JK	28	F	urban	housewife	No	No	No	No	Yes	06-06-2020	15	Yes	No	No	No	No	No	1	Yes	No	No	No	No	No	6	25	Yes
10	SK	20	F	rural	Student	No	No	No	Yes	No	10-06-2020	20	No	Yes	No	No	No	No	4	No	No	No	Yes	No	No	1	17	Yes
11	DK	18	M	urban	student	No	No	Yes	No	No	15-06-2020	17	Yes	No	No	No	No	No	4	No	No	No	Yes	No	No	5	15	Yes
12	R	26	F	urban	housewife	No	No	No	Yes	No	16-06-2020	20	No	Yes	No	No	No	No	1	Yes	No	No	No	No	No	2	20	Yes
13	SS	26	M	rural	farmer	No	No	No	Yes	No	17-06-2020	20	No	Yes	No	No	No	No	1	Yes	No	No	No	No	No	2	20	Yes
14	SK	28	M	urban	mechanic	No	No	No	Yes	No	23-06-2020	10	Yes	No	No	No	No	No	1	Yes	No	No	No	No	No	3	12	Yes
15	VK	27	M	rural	Env. Executive at DMCH	No	Yes	No	No	No	01-07-2020	27	No	Yes	No	No	No	No	3	No	No	Yes	No	No	No	1	23	Yes
16	PL	53	M	urban	shopkeeper	No	No	Yes	No	No	02-07-2020	52	No	No	No	No	Yes	No	1	Yes	No	No	No	No	No	1	52	Yes
17	IS	37	M	rural	farmer	No	No	Yes	No	No	08-07-2020	36	No	No	Yes	No	No	No	1	Yes	No	No	No	No	No	2	32	Yes
18	SK	26	F	urban	housewife	No	No	No	Yes	No	20-07-2020	24	No	Yes	No	No	No	No	1	Yes	No	No	No	No	No	3	5	Yes
19	HK	21	F	rural	Student	No	Yes	No	No	No	07-08-2020	6	Yes	No	No	No	No	No	4	No	No	No	Yes	No	No	1	19	Yes
20	RK	24	F	urban	Student	No	No	Yes	No	No	08-08-2020	24	No	Yes	No	No	No	No	4	No	No	No	Yes	No	No	4	20	Yes
21	SK	26	F	urban	Teacher	No	No	Yes	No	No	10-08-2020	22	No	Yes	No	No	No	No	4	No	No	No	Yes	No	No	2	20	Yes
22	GS	20	M	rural	shopkeeper	No	No	Yes	No	No	26-08-2020	18	Yes	No	No	No	No	No	1	Yes	No	No	No	No	No	2	15	Yes
23	Jk	28	F	rural	housewife	No	No	No	Yes	No	16-09-2020	5	Yes	No	No	No	No	No	1	Yes	No	No	No	No	No	3	26	Yes
24	SR	50	M	rural	Constrution worker	No	No	Yes	No	No	18-09-2020	49	No	No	No	Yes	No	No	1	Yes	No	No	No	No	No	4	49	Yes
25	AB	20	M	urban	Student	No	No	Yes	No	No	01-11-2020	15	Yes	No	No	No	No	No	1	Yes	No	No	No	No	No	3	16	Yes
26	KK	28	F	rural	housewife	No	No	No	Yes	No	03-11-2020	18	Yes	No	No	No	No	No	1	Yes	No	No	No	No	No	4	20	Yes
27	A	28	F	rural	housewife	No	No	No	Yes	No	11-11-2020	12	Yes	No	No	No	No	No	1	Yes	No	No	No	No	No	1	20	Yes
28	DS	28	M	rural	shopkeeper	No	No	Yes	No	No	15-11-2020	20	No	Yes	No	No	No	No	1	Yes	No	No	No	No	No	3	20	Yes
29	SK	35	M	urban	Patwari	No	No	Yes	No	No	16-11-2020	34	No	No	Yes	No	No	No	2	No	Yes	No	No	No	No	2	34	Yes
30	BS	38	M	rural	Driver	No	No	No	No	No	01-12-2021	37	No	No	Yes	No	No	No	6	No	No	No	No	No	Yes	1		Yes
31	PS	28	M	urban	Electrician	No	No	Yes	No	No	14-12-2020	25	No	Yes	No	No	No	No	6	No	No	No	No	No	Yes	2		Yes
32	J	25	M	urban	Student	No	No	Yes	No	No	20-12-2020	24	No	Yes	No	No	No	No	6	No	No	No	No	No	Yes	1	20	Yes
33	BK	18	F	rural	Student	No	Yes	No	No	Yes	26-12-2020	17	Yes	No	No	No	No	No	1	Yes	No	No	No	No	No	1	13.5	Yes
34	HK	18	F	urban	Student	No	No	Yes	No	No	02-01-2021	14	Yes	No	No	No	No	No	6	No	No	No	No	No	Yes	11	14	Yes
35	KS	26	M	urban	Advocate	No	Yes	No	No	No	14-01-2021	24	No	Yes	No	No	No	No	1	Yes	No	No	No	No	No	2	26	Yes
36	SS	33	M	rural	Pharmacist	No	Yes	No	No	No	15-01-2021	33	No	No	Yes	No	No	No	1	Yes	No	No	No	No	No	1	33	Yes
37	AK	18	F	urban	Student	No	No	Yes	No	No	01-01-2021	16	Yes	No	No	No	No	No	1	Yes	No	No	No	No	No	2	14	Yes
38	KK	18	M	urban	Student	No	Yes	No	No	No	15-01-2021	12	Yes	No	No	No	No	No	1	Yes	No	No	No	No	No	3	12	Yes
39	SS	47	M	rural	Shopkeeper	No	No	Yes	No	No	13-01-2021	44	No	No	No	Yes	No	No	1	Yes	No	No	No	No	No	4	35	Yes
40	HK	18	F	urban	Student	No	No	Yes	No	No	20-01-2021	13	No	No	No	No	No	No	4	No	No	No	Yes	No	No	2	16	Yes
41	SS	50	M	rural	farmer	No	No	Yes	No	No	12-01-2021	49	No	No	No	Yes	No	No	4	No	No	No	Yes	No	No	1	30	Yes
42	NK	25	M	urban	Student	No	No	No	Yes	No	18-02-2021	25	No	Yes	No	No	No	No	1	Yes	No	No	No	No	No	1	16	Yes
43	MK	28	F	urban	Teacher	No	Yes	No	No	No	22-02-2021	28	No	Yes	No	No	No	No	4	No	No	No	Yes	No	No	3	28	Yes
44	MS	38	M	rural	farmer	No	No	Yes	No	No	08-03-2021	36	No	No	Yes	No	No	No	6	No	No	No	No	No	Yes	3	36	Yes
45	NK	18	F	urban	Student	No	No	No	Yes	No	11-03-2021	18	Yes	No	No	No	No	No	5	No	No	No	No	Yes	No	4	12.5	Yes
46	MK	31	F	urban	housewife	No	No	Yes	No	No	12-03-2021	29	No	Yes	No	No	No	No	4	No	No	No	Yes	No	No	3	31	Yes
47	AS	18	M	urban	Student	No	No	Yes	No	No	12-03-2021	18	Yes	No	No	No	No	No	1	Yes	No	No	No	No	No	2	18	Yes
48	MK	32	F	rural	housewife	No	No	No	Yes	No	30-03-2021	21	No	Yes	No	No	No	No	1	Yes	No	No	No	No	No	2	32	Yes
49	SK	33	F	rural	housewife	No	No	Yes	No	No	01-04-2021	30	No	Yes	No	No	No	No	6	No	No	No	No	No	Yes	6	25	Yes
50	BK	18	F	urban	Student	No	No	Yes	No	No	05-04-2021	17	Yes	No	No	No	No	No	1	Yes	No	No	No	No	No	11	15	Yes
51	TS	35	M	rural	Travel agent	No	No	Yes	No	No	06-04-2021	35	No	No	Yes	No	No	No	1	Yes	No	No	No	No	No	1	30	Yes
52	MK	36	M	urban	Painter	No	No	Yes	No	No	18-05-2021	36	No	No	Yes	No	No	No	3	No	No	Yes	No	No	No	4	32	Yes
53	AR	18	M	urban	machin worker	No	No	No	Yes	No	21-06-2021	4	Yes	No	No	No	No	No	4	No	No	No	Yes	No	No	4	12	Yes
54	KS	32	M	rural	farmer	No	No	Yes	No	No	01-07-2021	31	No	No	Yes	No	No	No	1	Yes	No	No	No	No	No	2	1.5	Yes
55	KS	58	M	urban	Clerical Job	No	No	Yes	No	No	01-01-2021		No	No	No	No	No	No	3	No	No	Yes	No	No	No	2		Yes
56	R	29	M	urban	official Data	No	Yes	No	No	No	02-02-2020	29	No	Yes	No	No	No	No	1	Yes	No	No	No	No	No	1		Yes
57	MK	52	F	rural	housewife	No	No	Yes	No	No	02-12-2019	52	No	No	No	No	Yes	No	1	Yes	No	No	No	No	No	2.5	48	Yes
58	AK	21	M	rural	farmer	No	No	No	Yes	No	02-04-2021	17	Yes	No	No	No	No	No	1	Yes	No	No	No	No	No	4	17	Yes
59	HK	53	F	rural	housewife	No	No	No	No	Yes	15-07-2020		No	No	No	No	No	No	1	Yes	No	No	No	No	No	1	46	Yes
60	MK	31	F	urban	housewife	No	No	Yes	No	No	01-12-2020	31	No	No	Yes	No	No	No	5	No	No	No	No	Yes	Yes	2	31	Yes
61	BR	40	F	urban	housewife	No	No	No	No	Yes	05-05-2021	40	No	No	Yes	No	No	No	4	No	No	No	Yes	No	No	2	40	Yes
62	SS	29	M	urban	Clerical Job	No	No	Yes	No	No	01-02-2021	25	No	Yes	No	No	No	No	1	Yes	No	No	No	No	No	3	19	Yes

S.No	Initials	Triggering factors Exp Sunlight	Loud sound	Stress	looking up	Exp Cold	Travelling	Mobile	Physical activity	Talking and laughing	skipping meals	Lack of sleep	Sz	Reflection	Work	Rise in BP	Drop in BP	None	Mig with aura	Mig without aura	FH Epi	Past History	GPE	SYS exam	Levetiracetam 15mg/kg	Levetiracetam 20mg/kg	Levetiracetam 18mg/kg	Levetiracetam 8mg/kg	Valproate +Sodium valproate 1200mg	Valproate +Sodium valproate 25mg/kg
1	YS	No	No	No	No	No	No	Yes	No	No	No	Yes	No	No	No	No	No	No	Yes	No	No	No	normal	normal	No	Yes	No	No	No	No
2	SM	No	No	Yes	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	Yes	No	Yes	No	normal	normal	No	Yes	No	No	No	No
3	A	Yes	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	normal	normal	No	Yes	No	No	No	No
4	IS	No	No	Yes	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	Yes	normal	normal	No	No	No	No	No	No
5	D	Yes	No	No	No	Yes	No	Yes	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	normal	normal	No	No	No	No	No	No
6	HK	Yes	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	Yes	normal	normal	No	No	Yes	No	No	No
7	SA	Yes	No	Yes	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	normal	normal	No	No	Yes	No	No	No
8	RK	No	No	Yes	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	Yes	normal	normal	Yes	No	No	No	No	No
9	JK	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	Yes	normal	normal	No	Yes	No	No	No	No
10	SK	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	Yes	No	normal	normal	Yes	No	No	No	No	No
11	DK	No	No	Yes	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	Yes	No	No	normal	normal	No	No	No	No	No	No
12	R	No	Yes	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	Yes	normal	normal	No	Yes	No	No	No	No
13	SS	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	Yes	No	Yes	normal	normal	No	No	No	No	No	No
14	SK	No	No	No	No	No	No	No	Yes	Yes	No	No	No	No	No	No	No	No	No	Yes	No	Yes	normal	normal	No	No	No	No	No	No
15	VK	No	No	Yes	No	No	Yes	No	No	No	Yes	No	No	No	No	No	No	No	No	Yes	No	No	normal	normal	No	No	No	No	No	No
16	PL	Yes	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	Yes	No	normal	normal	No	No	No	No	No	No
17	IS	No	No	Yes	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	Yes	normal	normal	No	No	No	No	No	No
18	SK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	Yes	normal	normal	No	Yes	No	No	No	No
19	HK	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	Yes	normal	normal	No	No	No	Yes	No	No
20	RK	No	No	No	No	Yes	No	No	No	No	Yes	No	No	No	No	No	No	No	Yes	No	No	No	normal	normal	No	No	No	No	No	No
21	SK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	Yes	normal	normal	No	Yes	No	No	No	No
22	GS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	Yes	normal	normal	No	No	No	No	No	Yes
23	Jk	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	Yes	normal	normal	No	Yes	No	No	No	No
24	SR	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	normal	normal	No	No	No	No	No	No
25	AB	No	Yes	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	Yes	normal	normal	No	No	No	No	Yes	No
26	KK	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	No	No	No	No	Yes	No	No	Yes	normal	normal	No	No	No	No	No	No
27	A	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	Yes	normal	normal	No	No	No	No	No	No
28	DS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	Yes	normal	normal	No	No	No	No	No	Yes
29	SK	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	Yes	No	Yes	normal	normal	No	No	No	No	No	No
30	BS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	normal	normal	No	No	No	No	No	No
31	PS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	Yes	normal	normal	No	Yes	No	No	No	No
32	J	Yes	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	normal	normal	No	Yes	No	No	No	No
33	BK	No	Yes	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	normal	normal	No	No	No	No	No	No
34	HK	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	Yes	normal	normal	No	No	No	No	No	No
35	KS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	Yes	normal	normal	No	No	No	No	No	No
36	SS	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No	No	Yes	No	No	No	normal	normal	No	Yes	No	No	No	No
37	AK	Yes	Yes	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	Yes	No	normal	normal	No	No	No	No	No	No
38	KK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	Yes	normal	normal	No	No	No	No	No	No
39	SS	Yes	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	Yes	normal	normal	No	No	No	No	No	No
40	HK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	Yes	No	Yes	normal	normal	No	No	No	No	No	No
41	SS	Yes	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	normal	normal	No	No	No	No	No	No
42	NK	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	Yes	No	normal	normal	Yes	No	No	No	No	No
43	MK	No	No	No	Yes	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	Yes	normal	normal	No	No	No	Yes	No	No
44	MS	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	Yes	normal	normal	No	No	No	No	No	No
45	NK	Yes	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	Yes	No	normal	normal	No	Yes	No	No	No	No
46	MK	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	Yes	normal	normal	No	No	No	No	No	No
47	AS	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	Yes	No	No	No	normal	normal	Yes	No	No	No	No	No
48	MK	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	Yes	Yes	normal	normal	No	No	No	No	No	No
49	SK	No	Yes	Yes	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	Yes	normal	normal	No	No	No	Yes	No	No
50	BK	Yes	Yes	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	normal	normal	No	No	No	No	No	No
51	TS	No	Yes	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	normal	normal	No	Yes	No	No	No	No
52	MK	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	Yes	No	No	No	normal	normal	No	No	No	No	No	No
53	AR	Yes	Yes	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	Yes	normal	normal	No	No	No	No	No	No
54	KS	Yes	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	normal	normal	No	No	No	No	No	No
55	KS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	normal	normal	No	Yes	No	No	No	No
56	R	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	normal	normal	No	Yes	No	No	No	No
57	MK	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	Yes	Yes	No	normal	normal	Yes	No	No	No	No	No
58	AK	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	Yes	No	normal	normal	No	No	No	No	No	No
59	HK	Yes	Yes	Yes	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	normal	normal	No	No	Yes	No	No	No
60	MK	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	normal	normal	No	No	No	No	No	No
61	BR	Yes	No	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	Yes	normal	normal	No	Yes	Yes	No	No	No
62	SS	Yes	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	normal	normal	No	No	No	No	No	No

S.No	Initials	Valproate +Sodium valproate 25mg/kg	Valproate +Sodium valproate 25mg/kg	Valproate +Sodium valproate 25mg/kg	Valproate +Sodium valproate 20mg/kg	Valproate +Sodium valproate 20mg/kg	Brivaracetam 100mg/day	Brivaracetam 200mg/day	Brivaracetam 100mg/day	Lacosamide 350mg/day	Lacosamide 100mg/day	Oxecarbazepine 900 - 1200mg/day			Oxecarbazepine 600mg/day		Topiramate 250mg/day	Phenytoin 6mg/kg	Phenytoin 6mg/kg	Phenytoin 3mg/kg	Phenytoin 3mg/kg	Carbamazepine 20mg/kg
1	YS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
2	SM	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
3	A	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
4	IS	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
5	D	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No
6	HK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
7	SA	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
8	RK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No	No
9	JK	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
10	SK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
11	DK	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No
12	R	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
13	SS	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
14	SK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
15	VK	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	Yes	No	No	No	No	No	No
16	PL	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No
17	IS	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
18	SK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
19	HK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
20	RK	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No
21	SK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
22	GS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
23	Jk	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
24	SR	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes
25	AB	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
26	KK	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
27	A	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
28	DS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
29	SK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No	No
30	BS	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	Yes	No	No	No	No	No	No
31	PS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
32	J	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
33	BK	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
34	HK	No	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No
35	KS	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
36	SS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
37	AK	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
38	KK	No	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No
39	SS	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
40	HK	No	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No
41	SS	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No
42	NK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
43	MK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
44	MS	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No
45	NK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
46	MK	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	Yes	No	No	No	No	No	No
47	AS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
48	MK	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	Yes	No	No	No	No	No	No
49	SK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
50	BK	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
51	TS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
52	MK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No
53	AR	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
54	KS	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
55	KS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
56	R	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
57	MK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
58	AK	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
59	HK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
60	MK	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No
61	BR	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
62	SS	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No

S.No	Initials	Carbamazepine 20mg/kg	Carbamazepine 15mg/kg	Clobazam 10mg	Clobazam 5mg	Clobazam 5mg	Propanolol 20mg	Propanolol 10mg	Naproxen	Naproxen+ Domperidone	Etizolam	Nicoumalone	Metroprolol 50mg	Prednisolone 20mg	Prednisolone 10mg	Prednisolone 1mg	Multivitamins	Estalopram	Telmisoulan	Asprin	Olmesartan
1	YS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
2	SM	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes
3	A	No	No	Yes	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No
4	IS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
5	D	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No
6	HK	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No
7	SA	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	Yes	No	No	No	No
8	RK	No	No	No	No	No	Yes	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No
9	JK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
10	SK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
11	DK	No	No	No	Yes	No	No	Yes	No	Yes	No	No	No	No	No	No	No	No	No	No	No
12	R	No	No	No	Yes	No	No	Yes	No	Yes	No	No	No	No	No	No	No	No	No	No	No
13	SS	No	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No	Yes	No	No	No	No
14	SK	Yes	No	No	Yes	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No
15	VK	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
16	PL	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No
17	IS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
18	SK	No	No	No	No	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	No	No	No	No
19	HK	No	No	No	Yes	Yes	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No
20	RK	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
21	SK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No
22	GS	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
23	Jk	No	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No
24	SR	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No
25	AB	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
26	KK	No	No	No	No	No	No	Yes	No	Yes	No	No	No	No	No	No	Yes	No	No	No	No
27	A	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No
28	DS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
29	SK	No	No	Yes	No	No	No	No	No	Yes	No	No	No	No	No	No	Yes	No	No	No	No
30	BS	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
31	PS	No	No	No	Yes	No	No	Yes	No	Yes	No	No	No	No	No	No	Yes	No	No	No	No
32	J	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
33	BK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No
34	HK	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No
35	KS	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
36	SS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No
37	AK	No	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No	Yes	No	No	No	No
38	KK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
39	SS	No	No	No	No	No	Yes	No	Yes	No	No	No	No	No	No	No	Yes	No	No	No	No
40	HK	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No
41	SS	No	No	No	No	Yes	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No
42	NK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No
43	MK	No	No	Yes	No	No	Yes	No	Yes	No	No	No	No	No	No	No	Yes	No	No	No	No
44	MS	No	No	Yes	No	No	Yes	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No
45	NK	No	No	No	No	No	No	No	No	No	No	No	No	Yes	Yes	Yes	No	No	No	No	No
46	MK	No	No	No	Yes	No	No	Yes	Yes	No	No	No	No	No	No	No	Yes	No	No	No	No
47	AS	No	No	No	No	No	No	Yes	No	No	No	No	Yes	No	No	No	No	No	No	No	No
48	MK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
49	SK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
50	BK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
51	TS	No	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No
52	MK	No	No	No	No	No	No	Yes	Yes	Yes	No	No	No	No	No	No	No	No	No	No	No
53	AR	Yes	No	Yes	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No
54	KS	No	No	No	No	No	No	No	No	No	Yes	Yes	No	No	No	No	No	No	No	No	No
55	KS	No	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No
56	R	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
57	MK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	Yes	Yes	No
58	AK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
59	HK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
60	MK	No	No	No	Yes	No	No	Yes	No	Yes	No	No	No	No	No	No	No	No	No	No	No
61	BR	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
62	SS	No	No	No	No	No	No	Yes	No	No	No	No	Yes	No	No	No	Yes	No	No	No	No

S.No	Initials	Prazosin 5mg	Amitriptyline	Acenocoumarol	Metformin 25mg	Pantaprazole 40mg	Ranitidine	Amlodipine	Poroxetine 25mg	Migraine Freq Month before	Visual analogue scale (at enrollment)	Global assessment of migraine severity (at enrollment)	Frequency (1st Month)	Whole Head	Unilateral	Frontal	Occipital	Temples	Disablity (at enrollment)	Visual analogue scale (1st month)
1	YS	No	No	No	No	No	No	No	No	12	4	2	6	No	No	No	No	No	yes	4
2	SM	No	No	No	No	No	No	No	No	3.5	8	4	3.5	No	No	No	Yes	No	yes	8
3	A	No	No	No	No	No	No	No	No	1.5	8	4	1.5	Yes	No	Yes	No	No	yes	7
4	IS	No	No	No	No	No	No	No	No	12.5	7	3	5.5	No	No	No	No	No	yes	7
5	D	No	No	No	No	No	No	No	No	30	9	5	30	No	No	Yes	No	No	yes	9
6	HK	No	No	No	No	No	No	No	No	3.5	8	5	1	No	No	No	No	No	yes	8
7	SA	No	Yes	No	No	No	No	No	No	12.5	8	5	2.5	No	No	Yes	No	No	yes	7
8	RK	No	No	No	No	No	No	No	No	11	6	3	1	Yes	No	No	No	No	yes	6
9	JK	No	No	No	No	No	No	No	No	1.5	7	3	1.5	Yes	No	No	No	No	yes	7
10	SK	No	No	No	No	No	No	No	No	30	7	6	30	Yes	No	No	No	No	yes	7
11	DK	No	No	No	No	No	No	No	No	12.5	9	5	3.5	Yes	No	No	No	No	yes	9
12	R	No	No	No	No	No	No	No	No	1.5	8	5	2.5	No	No	Yes	No	No	yes	8
13	SS	No	No	No	No	No	No	No	No	30	10	6	0	No	No	No	No	No	no	0
14	SK	No	No	No	No	No	No	No	No	17.5	7	3	14	Yes	No	No	No	No	yes	7
15	VK	No	No	No	No	No	No	No	No	1.5	5	3	1.5	No	No	No	Yes	No	yes	6
16	PL	Yes	No	No	Yes	No	No	No	Yes	30	5	3	16.5	Yes	No	No	No	No	yes	5
17	IS	No	No	No	No	No	No	No	No	12.5	7	4	5.5	No	No	No	No	No	yes	7
18	SK	No	No	No	No	No	No	No	No	30	10	6	11	Yes	No	No	No	No	yes	4
19	HK	No	No	No	No	No	No	No	No	27.5	8	4	27.5	No	Yes	No	No	No	yes	8
20	RK	No	No	No	No	No	No	No	No	4.5	9	6	4.5	No	No	No	No	Yes	yes	9
21	SK	No	No	No	No	No	No	No	No	2.5	6	3	0	No	No	No	No	No	no	0
22	GS	No	No	No	No	No	No	No	No	11	3	2	0	No	No	No	No	No	no	0
23	Jk	No	No	No	No	No	No	No	No	9.5	8	5	4.5	No	No	No	Yes	Yes	yes	8
24	SR	No	No	No	No	No	No	No	No	4	10	6	0	No	No	No	No	No	no	0
25	AB	No	No	No	No	No	No	No	No	11	6	3	11	Yes	No	No	No	No	yes	9
26	KK	No	No	No	No	No	No	No	No	17.5	10	6	17.5	No	Yes	No	Yes	No	yes	10
27	A	No	No	No	No	No	No	No	No	12.5	3	2	2.5	No	No	No	No	Yes	no	3
28	DS	No	No	No	No	No	No	No	No	2.5	7	5	2.5	No	No	Yes	No	No	yes	7
29	SK	No	No	No	No	No	No	No	No	3.5	6	3	3.5	No	No	No	No	No	yes	6
30	BS	No	No	No	No	No	No	No	No	2	2	1	0	No	No	No	No	No	yes	0
31	PS	No	No	No	No	No	No	No	No	11	6	3	11	No	Yes	No	No	No	yes	6
32	J	No	No	Yes	No	No	No	No	No	2.5	8	4	1.5	No	Yes	No	No	No	yes	6
33	BK	No	No	No	No	No	No	No	No	3.5	9	6	3.5	Yes	No	No	No	No	yes	7
34	HK	No	No	No	No	No	No	No	No	6.5	4	3	0	No	No	No	No	No	no	0
35	KS	No	No	No	No	No	No	No	No	24	7	5	30	No	No	No	Yes	No	yes	7
36	SS	No	No	No	No	Yes	No	No	No	1	2	1	0	No	No	No	No	No	no	0
37	AK	No	No	No	No	No	No	No	No	12.5	9	6	2.5	Yes	Yes	No	No	No	yes	7
38	KK	No	No	No	No	No	No	No	No	12.5	9	6	0	No	No	No	No	No	no	0
39	SS	No	No	No	No	No	No	No	No	11.5	8	5	4.5	Yes	No	No	No	No	no	4
40	HK	No	No	No	No	No	No	No	No	1.5	4	3	0	No	No	No	No	No	no	0
41	SS	No	No	No	No	No	No	No	No	4.5	6	4	4.5	No	Yes	No	No	No	yes	6
42	NK	No	No	No	No	No	No	No	No	10	8	5	10	Yes	No	No	No	No	yes	8
43	MK	No	No	No	No	No	No	No	No	15	0	0	11	No	No	Yes	No	No	yes	8
44	MS	No	No	No	No	No	No	No	No	6.5	8	5	6.5	Yes	No	No	Yes	No	yes	8
45	NK	No	No	No	No	Yes	No	No	No	2.5	8	5	2.5	Yes	No	No	No	No	yes	8
46	MK	No	No	No	No	No	No	No	No	1.5	6	3	1.5	No	No	Yes	No	No	yes	6
47	AS	No	No	No	No	No	No	No	No	9	9	6	4.5	Yes	No	No	No	No	yes	7
48	MK	No	No	No	No	No	No	No	No	17.5	3	2	17.5	No	No	Yes	No	No	yes	7
49	SK	No	No	No	No	No	No	No	No	1.5	7	5	1.5	Yes	No	No	No	No	yes	7
50	BK	No	No	No	No	No	No	No	No	17.5	7	5	11	No	No	Yes	No	No	yes	7
51	TS	No	No	No	No	No	No	No	No	12.5	8	5	6.5	No	No	No	No	Yes	yes	4
52	MK	No	No	No	No	No	No	No	No	9	4	2	2	No	No	No	No	No	no	4
53	AR	No	No	No	No	No	No	No	No	19	8	5	11	Yes	No	No	No	No	yes	8
54	KS	No	No	No	No	No	Yes	No	No	2.5	5	3	2.5	No	No	Yes	No	No	yes	5
55	KS	No	No	No	No	No	No	No	No	1.5	2	1	1.5	No	No	No	No	No	yes	2
56	R	No	No	No	No	No	No	No	No	4.5	8	6	4	No	Yes	No	No	No	yes	5
57	MK	No	No	No	No	No	No	No	No	11	8	6	10	No	No	No	No	Yes	yes	9
58	AK	No	No	No	No	No	No	No	No	5	2	1	3.5	No	No	No	No	No	no	2
59	HK	No	No	No	No	No	No	No	No	2.5	4	2	2.5	No	No	Yes	No	No	no	4
60	MK	No	No	No	No	No	No	No	No	3	8	5	1.5	Yes	No	No	No	No	yes	8
61	BR	No	No	Yes	No	No	No	No	No	2.5	10	7	2.5	Yes	No	No	No	No	yes	10
62	SS	No	No	No	No	No	No	No	No	30	8	4	5.5	No	No	No	Yes	Yes	no	4

S.No	Initials	Global assessment of migraine severity (1st month)	Frequency (2nd month)	Whole Head	Unilateral	Frontal	Occipital	Temples	Disablity (1st month)	Visua analogue scale (2nd month)	Global assessment of migraine severity (2nd month)	Frequency (3rd month)	Whole Head	unilateral	Frontal	Occipital	Temples	Disablity (3rd month)	Visual analogue scale (3rd month)	Global assessment of migraine severity (3rd month)
1	YS	3	1.5	No	No	Yes	No	No	yes	4	3	3.5	No	No	Yes	No	No	no	4	3
2	SM	5	1.5	No	No	No	Yes	No	yes	8	5	1.5	No	No	No	Yes	No	yes	8	5
3	A	4	1	Yes	No	No	No	No	yes	7	4	0	No	No	No	No	No	no	0	0
4	IS	4	1.5	No	No	No	No	No	yes	5	3	0	No	No	No	No	No	no	0	0
5	D	6	30	No	No	Yes	No	No	yes	6	4	4.5	No	No	Yes	No	No	yes	2	1
6	HK	5	0	No	No	No	No	No	no	0	0	0	No	No	No	No	No	no	0	0
7	SA	5	2.5	No	No	Yes	No	No	yes	7	4	0	No	No	No	No	No	no	0	0
8	RK	3	1	Yes	No	No	No	No	yes	6	3	0	No	No	No	No	No	no	0	0
9	JK	4	3	Yes	No	No	No	No	yes	7	4	2	Yes	No	No	No	No	yes	7	4
10	SK	4	10	Yes	No	No	No	No	yes	7	4	8	Yes	No	No	No	No	yes	7	4
11	DK	6	3.5	Yes	No	No	No	No	yes	9	6	3.5	Yes	No	No	No	No	yes	9	6
12	R	6	2.5	No	No	Yes	No	No	yes	6	4	2.5	No	No	Yes	No	No	yes	5	3
13	SS	0	0	No	No	No	No	No	no	0	0	0	No	No	No	No	No	no	0	0
14	SK	4	12.5	Yes	No	No	No	No	yes	7	3	9	Yes	No	No	No	No	yes	7	3
15	VK	5	1	No	No	No	Yes	No	yes	5	4	1.5	No	No	No	Yes	No	yes	5	4
16	PL	3	15	Yes	No	No	No	No	yes	5	3	7.5	Yes	No	No	No	No	yes	4	2
17	IS	4	1.5	No	No	No	No	No	yes	5	3	0	No	No	No	No	No	no	0	0
18	SK	2	11	Yes	No	No	No	No	yes	4	2	17.5	Yes	No	No	No	No	yes	6	4
19	HK	4	7.5	No	Yes	No	No	No	no	5	4	2.5	No	Yes	No	No	No	no	3	2
20	RK	5	2.5	No	No	No	No	Yes	yes	9	6	2.5	No	No	No	No	Yes	yes	9	5
21	SK	0	0	No	No	No	No	No	no	0	0	0	No	No	No	No	No	no	0	0
22	GS	0	0	No	No	No	No	No	no	0	0	0	No	No	No	No	No	no	0	0
23	Jk	5	2.5	No	No	No	Yes	Yes	yes	8	5	2.5	No	No	No	Yes	Yes	yes	8	5
24	SR	0	0	No	No	No	No	No	no	0	0	0	No	No	No	No	No	no	0	0
25	AB	4	9	Yes	No	No	No	No	yes	6	4	9	Yes	No	No	No	No	yes	6	4
26	KK	6	11	No	Yes	No	Yes	No	yes	10	6	3.5	No	Yes	No	Yes	No	yes	8	4
27	A	1	1	No	No	No	No	Yes	no	3	1	2	No	No	No	No	Yes	no	3	1
28	DS	5	2.5	No	No	Yes	No	No	yes	7	5	2.5	No	No	Yes	No	No	yes	7	5
29	SK	3	2.5	No	No	No	No	No	yes	6	3	0.5	No	No	No	No	No	yes	6	3
30	BS	0		No	No	No	No	No	no	0	0		No	No	No	No	No	no	0	0
31	PS	4	4.5	No	Yes	No	No	No	yes	6	4	0	No	No	No	No	No	no	0	0
32	J	3	1	No	Yes	No	No	No	yes	6	3	1	No	Yes	No	No	No	yes	6	3
33	BK	3	1	Yes	No	No	No	No	yes	6	3	1	Yes	No	No	No	No	yes	6	3
34	HK	0	0	No	No	No	No	No	no	0	0	0	No	No	No	No	No	no	0	0
35	KS	4	30	No	No	No	Yes	No	yes	7	4	30	No	No	No	Yes	No	yes	7	4
36	SS	0	0	No	No	No	No	No	no	0	0	0	No	No	No	No	No	no	0	0
37	AK	4	2.5	Yes	Yes	No	No	No	yes	7	4	2.5	No	Yes	No	No	No	yes	7	4
38	KK	0	0	No	No	No	No	No	no	0	0	0	No	No	No	No	No	no	0	0
39	SS	2	4.5	Yes	No	No	No	No	no	4	2	1.5	Yes	No	No	No	No	no	4	2
40	HK	0	0	No	No	No	No	No	no	0	0	0	No	No	No	No	No	no	0	0
41	SS	4	2	No	Yes	No	No	No	yes	6	4	4	No	Yes	No	No	No	yes	6	3
42	NK	5	7	Yes	No	No	No	No	no	5	3	4	Yes	No	No	No	No	no	5	3
43	MK	5	4.5	No	No	Yes	No	No	yes	5	2	4.5	No	No	Yes	No	No	yes	5	2
44	MS	5	6.5	Yes	No	No	Yes	No	yes	8	5	6.5	Yes	No	No	Yes	No	yes	8	5
45	NK	5	2.5	Yes	No	No	No	No	yes	8	5	1.5	Yes	No	No	No	No	yes	8	5
46	MK	3	1.5	No	No	Yes	No	No	yes	6	3	1.5	No	No	Yes	No	No	yes	6	3
47	AS	3	4	Yes	No	No	No	No	yes	7	3	0	No	No	No	No	No	no	0	0
48	MK	4	9.5	No	No	Yes	No	No	yes	4	2	9.5	No	No	Yes	No	No	yes	4	2
49	SK	4	1.5	Yes	No	No	No	No	yes	7	4	1.5	Yes	No	No	No	No	yes	7	4
50	BK	3	11	No	No	Yes	No	No	yes	7	3	11	No	No	Yes	No	No	yes	7	3
51	TS	2	2	No	No	No	No	Yes	yes	4	2	2.5	No	No	No	No	Yes	yes	4	2
52	MK	2	0	No	No	No	No	No	no	o	o	o	No	No	No	No	No	no	0	0
53	AR	4	0	No	No	No	No	No	no	o	o	o	No	No	No	No	No	no	0	0
54	KS	2	1	No	No	Yes	No	No	yes	5	2	2	No	No	Yes	No	No	yes	5	2
55	KS	1	1.5	No	No	No	No	No	yes	2	1	0	No	No	No	No	No	no	0	0
56	R	2	4	No	Yes	No	No	No	yes	5	2	4	No	Yes	No	No	No	yes	5	2
57	MK	6	4.5	No	No	No	No	Yes	yes	7	3	4.5	No	No	No	No	Yes	yes	7	3
58	AK	1	3	No	No	No	No	No	no	2	1	3	No	No	No	No	No	no	2	1
59	HK	2	0	No	No	No	No	No	no	0	0	0	No	No	No	No	No	no	0	0
60	MK	6	1	Yes	No	No	No	No	yes	7	5	0	No	No	No	No	No	no	0	0
61	BR	7	1.5	Yes	No	No	No	No	yes	10	7	0	No	No	No	No	No	no	0	0
62	SS	2	3.5	No	No	No	No	Yes	no	4	2	3.5	No	No	No	No	Yes	no	4	2

S.No	Initials	Age	gender	Residence	Occupation	SE Status Upper	Upper middle	lower middle	Upper lower	lower	Enrollment Date	Age Onset Epi	Age Onset Epi Range 11-20yrs	21-30yrs	31-40yrs	41-50yrs	51-60yrs	Epi Dur Enroll	Semiology	GTCS	Myoclonic	Focal Motor	CPS	SPS	Focal with Sec. Generalization	Freq Sz	Age Onset Mig	Mig Dur Enroll
63	RK	23	F	rural	housewife	No	No	Yes	No	No	01-05-2021	20	Yes	No	No	No	No	No	5	No	No	No	No	Yes	No	2.5	20	Yes
64	RK	20	F	urban	Student	No	No	No	No	No	10-03-2021	12	Yes	No	No	No	No	No	5	No	No	No	No	Yes	No	9.5	18	Yes
65	HS	19	M	urban	Student	No	No	No	No	Yes	01-04-2021	18	Yes	No	No	No	No	No	1	Yes	No	No	No	No	No	7.5	17	Yes
66	HS	32	M	urban	labour	No	No	No	No	Yes	23-12-2020	31	No	No	Yes	No	No	No	5	No	No	No	No	Yes	No	5	31	Yes
67	P	58	F	rural	housewife	No	No	Yes	No	No	13-07-2020	47	No	No	No	Yes	No	No	4	No	No	No	Yes	No	Yes	2	45	Yes
68	AS	36	M	urban	shopkeeper	No	Yes	No	No	No	07-09-2020		No	No	Yes	No	No	No	4	No	No	No	Yes	No	Yes	2	35	Yes
69	HS	45	M	urban	poen	No	No	No	Yes	No		45	No	No	No	Yes	No	No	1	Yes	No	No	No	No	No	1	43	Yes
70	AK	26	M	rural	shopkeeper	No	Yes	No	No	No	25-07-2021	22	No	Yes	No	No	No	No	1	Yes	No	No	No	No	No	4.5	22	Yes
71	HK	21	F	urban	Student	No	No	Yes	No	No	01-08-2020	16	Yes	No	No	No	No	No	4	No	No	No	Yes	No	No	1	19	Yes
72	SK	26	F	rural	housewife	No	No	No	Yes	No	01-01-2021	14	Yes	No	No	No	No	No	4	No	No	No	Yes	No	No	4.5	14	Yes
73	R	19	F	urban	Student	No	No	Yes	No	No	01-01-2020	19	Yes	No	No	No	No	No	4	No	No	No	Yes	No	No	5	17	Yes
74	H	50	M	rural	civil engineer	No	Yes	No	No	No	01-12-2020	45	No	No	No	Yes	No	No	1	Yes	No	No	No	No	No	1	45	Yes
75	R	30	M	urban	shopkeeper	No	No	No	Yes	No	05-10-2021	17	Yes	No	No	No	No	No	1	Yes	No	No	No	No	No	6.5	20	Yes
76	NK	20	F	rural	Student	No	No	No	No	Yes	01-04-2020	12	Yes	No	No	No	No	No	5	No	No	No	No	Yes	No	5.5	18	Yes
77	LS	23	M	rural	Student	No	No	No	Yes	No	01-10-2020	20	Yes	No	No	No	No	No	1	Yes	No	No	No	No	No	2.5	20	Yes
78	RS	39	M	urban	shopkeeper	No	No	Yes	No	No	01-01-2021	38	No	No	Yes	No	No	No	1	Yes	No	No	No	No	No	1	38	Yes
79	SK	27	F	rural	housewife	No	No	Yes	No	No	01-05-2021	20	Yes	No	No	No	No	No	2	No	Yes	No	No	No	No	3	17	Yes
80	SK	39	F	urban	housewife	No	No	No	No	Yes	01-05-2020	34	No	No	Yes	No	No	No	2	No	Yes	No	No	No	No	2	34	Yes
81	AS	18	M	urban	Student	No	No	No	Yes	No	01-04-2021	16	Yes	No	No	No	No	No	5	No	No	No	No	Yes	No	3	17	Yes
82	GS	31	F	urban	Teacher	No	Yes	No	No	No	01-01-2021	27	No	Yes	No	No	No	No	4	No	No	No	Yes	No	No	4	27	Yes
83	BS	18	M	rural	Student	No	No	Yes	No	No	01-03-2021	17	Yes	No	No	No	No	No	1	Yes	No	No	No	No	No	3	16	Yes
84	SS	51	M	rural	shopkeeper	No	No	No	Yes	No	01-05-2021	31	No	No	Yes	No	No	No	4	No	No	No	Yes	No	No	2	31	Yes
85	KS	41	M	urban	shopkeeper	No	No	Yes	No	No	01-02-2021	30	No	Yes	No	No	No	No	4	No	No	No	Yes	No	No	1.5	30	Yes
86	RR	37	F	urban	housewife	No	No	Yes	No	No	01-01-2021	24	No	Yes	No	No	No	No	1	Yes	No	No	No	No	No	10	30	Yes
87	MS	62	M	urban	farmer	No	No	Yes	No	Yes	01-05-2021		No	No	No	No	No	No	1	Yes	No	No	No	No	No			Yes
88	AK	18	F	urban	Student	No	No	Yes	No	No	01-01-2021	16	Yes	No	No	No	Yes	No	4	No	No	No	Yes	No	No	2	14	Yes
89	JS	20	M	rural	farmer	No	No	No	Yes	No	02-04-2021	17	Yes	No	No	No	No	No	3	No	No	Yes	No	No	Yes	4	17	Yes
90	R	29	F	urban	housewife	No	Yes	No	No	No	01-05-2021	17	Yes	No	No	No	No	No	1	Yes	No	No	No	No	No	3	17	Yes
91	AR	18	M	urban	Student	No	No	Yes	No	No	01-06-2021	14	Yes	No	No	No	No	No	1	Yes	No	No	No	No	No	4	12	Yes
92	BS	55	M	rural	labour	No	No	No	Yes	No	01-04-2021		No	No	No	No	No	No	1	Yes	No	No	No	No	No			Yes
93	AS	55	M	urban	sealsman	No	No	Yes	No	No	01-05-2021	51	No	No	No	No	Yes	No	5	No	No	No	No	Yes	No	2	51	Yes
94	MB	30	F	urban	housewife	No	Yes	No	No	No			No	No	No	No	No	No	5	No	No	No	No	Yes	No	1		Yes
95	SR	19	F	urban	Student	No	Yes	No	No	No	01-04-2021	17	Yes	No	No	No	No	No	1	Yes	No	No	No	No	No	2.5	17	Yes
96	MK	28	F	urban	Teacher	No	Yes	No	No	No	22-02-2021	28	No	Yes	No	No	No	No	1	Yes	No	No	No	No	No	3	28	Yes
97	HK	26	M	rural	farmer	No	Yes	Yes	No	No	20-09-2021	18	Yes	No	No	No	No	No	1	Yes	No	No	No	No	No	4		Yes
98	KK	26	F	rural	housewife	No	Yes	Yes	No	No	01-02-2021	23	No	Yes	No	No	No	No	4	No	No	No	Yes	No	No	2.5	24	Yes
99	H	36	M	urban	sales reprentative	No	Yes	Yes	No	No	01-07-2020	36	No	No	Yes	No	No	No	5	No	No	No	No	Yes	No	1	33	Yes
100	RS	34	M	urban	car repair	No	No	Yes	No	No	10-03-2021	33	No	No	Yes	No	No	No	5	No	No	No	No	Yes	No	2	30	Yes
101	AS	18	M	rural	Student	No	No	No	Yes	No	01-04-2021	16	Yes	No	No	No	No	No	5	No	No	No	No	Yes	No	3	17	Yes
102	HS	32	M	urban	labour	No	No	Yes	No	No	23-12-2020	31	No	No	Yes	No	No	No	1	Yes	No	No	No	No	No	5	31	Yes

S.No	Initials	Triggering factors Exp Sunlight	Loud sound	Stress	looking up	Exp Cold	Travelling	Mobile	Physical activity	Talking and laughing	skipping meals	Lack of sleep	Sz	Reflection	Work	Rise in BP	Drop in BP	None	Mig with aura	Mig without aura	FH Epi	Past History	GPE	SYS exam	Levetiracetam 15mg/kg	Levetiracetam 20mg/kg	Levetiracetam 18mg/kg	Levetiracetam 8mg/kg	Valproate +Sodium valproate 1200mg	Valproate +Sodium valproate 25mg/kg
63	RK	Yes	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	Yes	No	normal	normal	No	No	No	Yes	No	No
64	RK	Yes	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	normal	normal	No	No	No	Yes	No	No
65	HS	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No	Yes	No	No	normal	normal	No	Yes	No	No	No	No
66	HS	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	normal	normal	No	No	No	No	No	No
67	P	No	No	Yes	No	No	Yes	No	No	No	No	Yes	No	No	No	No	No	No	No	Yes	Yes	Yes	normal	normal	No	No	No	No	No	No
68	AS	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	normal	normal	No	No	No	No	No	No
69	HS	No	Yes	Yes	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	Yes	Yes	No	normal	normal	Yes	No	No	No	No	No
70	AK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	Yes	No	Yes	Yes	normal	normal	No	No	No	No	No	No
71	HK	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	Yes	normal	normal	No	No	No	Yes	No	No
72	SK	Yes	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	normal	normal	No	No	No	No	No	No
73	R	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	normal	normal	No	No	No	No	No	No
74	H	No	No	Yes	No	Yes	Yes	No	No	No	No	No	No	No	Yes	No	No	No	No	Yes	Yes	Yes	normal	normal	No	Yes	No	No	No	No
75	R	No	No	Yes	No	No	Yes	Yes	No	No	No	Yes	No	No	No	No	No	No	No	Yes	No	No	normal	normal	No	No	No	No	No	Yes
76	NK	No	Yes	Yes	No	No	Yes	No	No	No	No	No	No	No	Yes	No	No	No	No	Yes	Yes	No	normal	normal	No	No	No	No	No	No
77	LS	No	No	No	No	No	Yes	No	No	No	No	Yes	No	No	No	No	No	No	No	Yes	No	No	normal	normal	No	No	No	No	No	Yes
78	RS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	Yes	No	No	No	normal	normal	No	No	No	No	No	No
79	SK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	Yes	No	No	normal	normal	No	No	No	No	No	No
80	SK	Yes	Yes	Yes	No	No	No	No	No	No	Yes	Yes	No	No	No	No	No	No	Yes	No	No	No	normal	normal	No	No	No	No	No	No
81	AS	No	No	Yes	No	No	No	No	No	No	No	Yes	No	No	Yes	No	No	No	No	Yes	No	No	normal	normal	Yes	No	No	No	No	No
82	GS	No	Yes	Yes	No	No	Yes	No	No	No	No	No	No	No	No	Yes	No	No	Yes	No	Yes	Yes	normal	normal	No	No	No	No	No	No
83	BS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	normal	normal	No	No	No	No	No	Yes
84	SS	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	Yes	Yes	No	normal	normal	No	Yes	No	No	No	No
85	KS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	normal	normal	No	Yes	No	No	No	No
86	RR	No	Yes	Yes	No	Yes	Yes	Yes	No	No	Yes	No	No	No	No	No	No	No	No	Yes	No	No	normal	normal	No	No	No	Yes	No	No
87	MS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	normal	normal	No	Yes	No	No	No	No
88	AK	Yes	Yes	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	Yes	No	normal	normal	No	No	No	No	No	No
89	JS	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	Yes	No	normal	normal	No	Yes	No	No	No	No
90	R	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	Yes	No	No	normal	normal	No	No	No	No	No	Yes
91	AR	Yes	Yes	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	Yes	normal	normal	No	No	No	No	No	No
92	BS	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	normal	normal	No	No	No	No	No	No
93	AS	Yes	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	Yes	No	normal	normal	Yes	No	No	No	No	No
94	MB	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	normal	normal	No	No	No	No	No	No
95	SR	Yes	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	normal	normal	No	No	No	No	No	No
96	MK	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	Yes	normal	normal	No	No	No	No	No	No
97	HK	Yes	No	Yes	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	Yes	No	No	normal	normal	No	No	No	No	No	No
98	KK	Yes	No	Yes	No	No	No	No	No	No	Yes	Yes	No	No	No	No	No	No	No	Yes	No	No	normal	normal	No	Yes	No	No	No	No
99	H	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	normal	normal	No	Yes	No	No	No	No
100	RS	No	No	Yes	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No	Yes	No	Yes	normal	normal	Yes	No	No	No	No	No
101	AS	No	No	Yes	No	No	No	No	No	No	No	Yes	No	No	Yes	No	No	No	No	Yes	No	No	normal	normal	Yes	No	No	No	No	No
102	HS	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	normal	normal	No	Yes	No	No	No	No

S.No	Initials	Valproate +Sodium valproate 25mg/kg	Valproate +Sodium valproate 25mg/kg	Valproate +Sodium valproate 25mg/kg	Valproate +Sodium valproate 20mg/kg	Valproate +Sodium valproate 20mg/kg	Brivaracetam 100mg/day	Brivaracetam 200mg/day	Brivaracetam 100mg/day	Lacosamide 350mg/day	Lacosamide 100mg/day	Oxecarbazepine 900 - 1200mg/day			Oxecarbazepine 600mg/day		Topiramate 250mg/day	Phenytoin 6mg/kg	Phenytoin 6mg/kg	Phenytoin 3mg/kg	Phenytoin 3mg/kg	Carbamazepine 20mg/kg
63	RK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
64	RK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
65	HS	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No
66	HS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
67	P	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No
68	AS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No
69	HS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
70	AK	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
71	HK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
72	SK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No
73	R	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No	Yes	No	No	No	No	No
74	H	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
75	R	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
76	NK	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No
77	LS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
78	RS	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No
79	SK	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
80	SK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No	No
81	AS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
82	GS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
83	BS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
84	SS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
85	KS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
86	RR	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
87	MS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
88	AK	No	Yes	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
89	JS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
90	R	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
91	AR	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
92	BS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No
93	AS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
94	MB	No	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No
95	SR	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
96	MK	No	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No
97	HK	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
98	KK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
99	H	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
100	RS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
101	AS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
102	HS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No

S.No	Initials	Carbamazepine 20mg/kg	Carbamazepine 15mg/kg	Clobazam 10mg	Clobazam 5mg	Clobazam 5mg	Propanolol 20mg	Propanolol 10mg	Naproxen	Naproxen+ Domperidone	Etizolam	Nicoumalone	Metroprolol 50mg	Prednisolone 20mg	Prednisolone 10mg	Prednisolone 1mg	Multivitamins	Estalopram	Telmisoulan	Asprin	Olmesartan
63	RK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No
64	RK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
65	HS	No	No	Yes	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No
66	HS	Yes	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
67	P	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No
68	AS	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
69	HS	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No
70	AK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No
71	HK	No	No	No	Yes	Yes	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No
72	SK	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
73	R	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
74	H	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
75	R	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
76	NK	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
77	LS	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No
78	RS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
79	SK	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
80	SK	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No
81	AS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
82	GS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
83	BS	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
84	SS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No
85	KS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
86	RR	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
87	MS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
88	AK	No	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No	Yes	No	No	No	No
89	JS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
90	R	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No
91	AR	Yes	No	Yes	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No
92	BS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
93	AS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
94	MB	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
95	SR	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
96	MK	No	No	Yes	No	No	No	Yes	No	Yes	No	No	No	No	No	No	Yes	No	No	No	No
97	HK	No	No	No	No	No	No	Yes	No	Yes	No	No	No	No	No	No	No	No	No	No	No
98	KK	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No
99	H	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No	Yes	No	No	No	No
100	RS	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
101	AS	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
102	HS	Yes	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No

S.No	Initials	Prazosin 5mg	Amitriptyline	Acenocoumarol	Metformin 25mg	Pantaprazole 40mg	Ranitidine	Amlodipine	Poroxetine 25mg	Migraine Freq Month before	Visual analogue scale (at enrollment)	Global assessment of migraine severity (at enrollment)	Frequency (1st Month)	Whole Head	Unilateral	Frontal	Occipital	Temples	Disablity (at enrollment)	Visual analogue scale (1st month)
63	RK	No	No	No	No	No	No	No	No	4	9	6	4	No	No	Yes	No	No	yes	9
64	RK	No	No	No	No	No	No	No	No	3.5	6	3	3.5	Yes	No	No	No	No	yes	6
65	HS	No	No	No	No	No	No	No	No	8	6	3	3	Yes	No	No	No	No	yes	6
66	HS	No	No	No	No	No	No	No	No	20	8	5	15	Yes	No	No	No	No	yes	6
67	P	No	No	No	No	No	No	No	No	4.5	8	5	4.5	No	Yes	No	No	No	yes	8
68	AS	No	No	No	No	No	No	No	No	5.5	6	3	5.5	No	No	No	Yes	No	yes	6
69	HS	No	No	No	No	No	No	No	No	9	8	5	9	Yes	No	No	No	No	yes	8
70	AK	No	No	No	No	No	No	No	No	2.5	6	3	2.5	Yes	No	No	No	No	yes	6
71	HK	No	No	No	No	No	No	No	No	27.5	8	5	27.5	No	Yes	No	No	No	yes	8
72	SK	No	No	No	No	No	No	No	No	4.5	8	5	4.5	Yes	No	No	No	No	yes	8
73	R	No	No	No	No	No	No	No	No	20	7	4	20	No	No	No	No	Yes	yes	7
74	H	No	No	No	No	No	No	No	No	2	5	2	2	Yes	No	No	No	No	yes	5
75	R	No	No	No	No	No	No	No	No	15	6	3	15	No	Yes	No	No	No	yes	6
76	NK	No	No	No	No	No	No	No	No	20	8	5	12.5	No	Yes	No	No	No	yes	8
77	LS	No	No	No	No	No	No	No	No	2.5	2	1	3.5	Yes	No	No	No	No	no	2
78	RS	No	No	No	No	No	No	No	No	1.5	3	2	1.5	Yes	No	No	No	No	yes	3
79	SK	No	No	No	No	No	No	No	No	12.5	5	3	12.5	Yes	No	No	No	No	yes	5
80	SK	No	No	No	No	No	No	No	No	30	10	6	30	Yes	No	No	No	No	yes	10
81	AS	No	No	No	No	No	No	No	No	15	3	1	4.5	No	No	Yes	No	No	yes	3
82	GS	No	No	No	No	No	No	No	No	30	8	5	30	Yes	No	No	No	No	yes	8
83	BS	No	No	No	No	No	No	No	No	5.5	7	4	5.5	Yes	No	No	No	No	yes	7
84	SS	No	No	No	No	No	No	No	No	3	3	2	5	Yes	No	No	No	No	no	2
85	KS	No	No	No	No	No	No	No	No	5.5	4	2	5.5	Yes	No	No	No	No	yes	4
86	RR	No	No	No	No	No	No	No	No	30	5	3	22.5	No	Yes	No	No	No	yes	5
87	MS	No	No	No	No	No	No	No	No	3	3	2	1.5	No	No	No	No	Yes	yes	3
88	AK	No	No	No	No	No	No	No	No	12.5	9	6	2.5	Yes	Yes	No	No	No	yes	7
89	JS	No	No	No	No	No	No	No	No	5	2	1	3.5	No	No	No	No	No	no	2
90	R	No	No	No	No	No	No	No	No	5.5	9	5	5.5	No	No	No	No	Yes	no	9
91	AR	No	No	No	No	No	No	No	No	19	8	4	11	Yes	No	No	No	No	no	8
92	BS	No	No	No	No	No	No	No	No	5	2	1	3.5	No	No	No	No	Yes	no	2
93	AS	No	No	No	No	No	No	Yes	No	1.5	2	1	1.5	No	No	No	No	No	no	1
94	MB	No	No	No	No	No	No	No	No	30	4	3	30	Yes	No	No	No	No	yes	4
95	SR	No	No	No	No	No	No	No	No	4	5	4	2.5	No	No	No	No	No	no	5
96	MK	No	No	No	No	No	No	No	No	15	5	4	11	No	No	Yes	No	No	yes	8
97	HK	No	No	No	No	No	No	No	No	3.5	9	5	3.5	No	Yes	No	No	No	yes	9
98	KK	No	No	No	No	No	No	No	No	30	10	6	30	No	No	Yes	No	Yes	no	10
99	H	No	No	No	No	Yes	No	No	No	4.5	8	4	4.5	No	No	No	No	No	yes	3
100	RS	No	No	No	No	Yes	No	No	No	17.5	8	4	17.5	Yes	Yes	No	No	No	no	8
101	AS	No	No	No	No	No	No	No	No	15	3	2	4.5	No	No	Yes	No	No	yes	3
102	HS	No	No	No	No	No	No	No	No	20	8	5	15	Yes	No	No	No	No	no	6

S.No	Initials	Global assessment of migraine severity (1st month)	Frequency (2nd month)	Whole Head	Unilateral	Frontal	Occipital	Temples	Disablity (1st month)	Visua analogue scale (2nd month)	Global assessment of migraine severity (2nd month)	Frequency (3rd month)	Whole Head	unilateral	Frontal	Occipital	Temples	Disablity (3rd month)	Visual analogue scale (3rd month)	Global assessment of migraine severity (3rd month)
63	RK	6	2.5	No	No	Yes	No	No	yes	8	4	2	No	No	Yes	No	No	yes	8	4
64	RK	4	2.5	Yes	No	No	No	No	yes	6	3	1.5	Yes	No	No	No	No	yes	6	3
65	HS	2	1.5	Yes	No	No	No	No	yes	6	2	0	No	No	No	No	No	no	0	0
66	HS	3	10	Yes	No	No	No	No	yes	6	3	10	Yes	No	No	No	No	yes	6	3
67	P	5	2.5	No	Yes	No	No	No	no	3	2	1	No	Yes	No	No	No	no	1	1
68	AS	3	1.5	No	No	No	Yes	No	yes	5	2	1.5	No	No	No	Yes	No	yes	5	2
69	HS	5	5.5	Yes	No	No	No	No	yes	7	3	0	No	No	No	No	No	no	0	0
70	AK	2	1	Yes	No	No	No	No	yes	6	2	0	No	No	No	No	No	no	0	0
71	HK	4	7.5	No	Yes	No	No	No	yes	5	4	2.5	No	Yes	No	No	No	yes	3	2
72	SK	5	2.5	Yes	No	No	No	No	yes	7	4	0	No	No	No	No	No	yes	0	0
73	R	4	17	No	No	No	No	Yes	yes	8	4	15	No	No	No	No	Yes	yes	7	3
74	H	3	0	No	No	No	No	No	no	0	0	0	No	No	No	No	No	no	0	0
75	R	3	6.5	No	Yes	No	No	No	yes	6	3	0	No	No	No	No	No	no	0	0
76	NK	4	7.5	No	Yes	No	No	No	yes	8	4	5.5	No	Yes	No	No	No	no	8	4
77	LS	1	1.5	Yes	No	No	No	No	no	2	1	0	No	No	No	No	No	no	0	0
78	RS	2	1.5	Yes	No	No	No	No	yes	3	2	0	No	No	No	No	No	no	0	0
79	SK	3	7.5	Yes	No	No	No	No	yes	5	3	7.5	Yes	No	No	No	No	no	5	3
80	SK	6	15	Yes	No	No	No	No	yes	8	4	8	Yes	No	No	No	No	yes	5	2
81	AS	2	2.5	No	No	Yes	No	No	yes	3	2	1	No	No	Yes	No	No	yes	2	1
82	GS	4	20	Yes	No	No	No	No	yes	8	4	7.5	Yes	No	No	No	No	no	8	4
83	BS	4	4.5	Yes	No	No	No	No	yes	7	4	3.3	Yes	No	No	No	No	no	5	3
84	SS	2	1	Yes	No	No	No	No	no	2	2	0	No	No	No	No	No	no	0	0
85	KS	2	4.5	Yes	No	No	No	No	yes	4	2	4.5	Yes	No	No	No	No	no	4	2
86	RR	3	15	No	Yes	No	No	No	yes	5	3	12	No	Yes	No	No	No	no	5	3
87	MS	2	1.5	No	No	No	No	Yes	yes	3	2	0	No	No	No	No	No	no	0	0
88	AK	4	2.5	Yes	Yes	No	No	No	yes	7	4	2.5	No	Yes	No	No	No	yes	7	4
89	JS	1	3	No	No	No	No	No	no	2	1	1	No	No	No	No	No	no	2	1
90	R	5	4.5	No	No	No	No	Yes	yes	9	5	2.5	No	No	No	No	Yes	yes	9	5
91	AR	4	9	Yes	No	No	No	No	yes	8	4	15	Yes	No	No	No	No	yes	8	4
92	BS	1	3	No	No	No	No	Yes	no	2	1	1	No	No	No	No	Yes	no	2	1
93	AS	1	1	No	No	No	No	No	no	1	1	0	No	No	No	No	No	no	0	0
94	MB	2	15	Yes	No	No	No	No	yes	4	2	20	Yes	No	No	No	No	yes	3	2
95	SR	2	2	No	No	No	No	No	no	5	2	2	No	No	No	No	No	no	5	2
96	MK	5	4.5	No	No	Yes	No	No	yes	5	2	3.5	No	No	Yes	No	No	no	5	2
97	HK	5	1.5	No	Yes	No	No	No	yes	9	5	1.5	No	Yes	No	No	No	no	8	5
98	KK	6	25	No	No	Yes	No	Yes	yes	10	6	10	No	No	Yes	No	Yes	no	10	6
99	H	2	4.5	No	No	No	No	No	no	3	1	2.5	No	No	No	No	No	no	2	1
100	RS	5	4.5	Yes	Yes	No	No	No	yes	8	5	4.5	Yes	Yes	No	No	No	no	8	5
101	AS	2	2.5	No	No	Yes	No	No	yes	3	2	1	No	No	Yes	No	No	yes	2	1
102	HS	3	10	Yes	No	No	No	No	yes	6	3	10	Yes	No	No	No	No	yes	6	3

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Date 20/4/2021

The Principal,
DMC,Ludhiana.

Subject: **Approval of Plan of Thesis.**

This is to inform you that the Faculty of Medical Sciences in its meeting held on 22.01.2021 has approved the plan of thesis of **Dr. Samriti Jain,** a student of your college for **MD Pharmacology** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis
To study the effect of antiepileptic drugs on migraine in patients with new onset epilepsy

Supervisor
Dr. Sandeep Kaushal
Prof. & Head,
Dept. of Pharmacology,
DMCH, Ludhiana.

Co-Supervisor
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The student has to submit the three copies of thesis (along with PDF format) , to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She must directed to attach a photocopy of this letter with the forwarding letter while submitting thesis to the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic.(if any).

S P Singh

Dr. S P Singh MS(Oph)
Controller of Examinations

Note :

1. ***If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.***
2. *The student may submit the thesis as per the schedule already conveyed i.e for May/June examination 30th Nov of the preceding the year of examination and for Nov/Dec examinations 31st May of the year of examination.*

TO STUDY THE EFFECT OF ANTIEPILEPTIC DRUGS ON MIGRAINE IN PATIENTS WITH NEW ONSET EPILEPSY

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

Doctor of Medicine

in

Pharmacology

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES

FARIDKOT

November, 2019

Dr. Samriti Jain

DEPARTMENT OF PHARMACOLOGY
DAYANAND MEDICAL COLLEGE AND HOSPITAL
LUDHIANA

ABSTRACT OF PLAN OF THESIS

Title	TO STUDY THE EFFECT OF ANTIEPILEPTIC DRUGS ON MIGRAINE IN PATIENTS WITH NEW ONSET EPILEPSY
For the degree of	MD Pharmacology
Name of the candidate	Dr. Samriti Jain
Supervisor	Dr. Sandeep Kaushal, Professor & Head, Department of Pharmacology, DMCH, Ludhiana
Co-supervisor	Dr. Shalini Arora, Professor, Department of Pharmacology, DMCH, Ludhiana Dr. Monika Singla, Associate Professor, Department of Neurology, DMCH, Ludhiana
Institution	Dayanand Medical College & Hospital, Ludhiana
University	Baba Farid University of Health Sciences, Faridkot

Introduction: There is an estimated 50 million people worldwide suffering from epilepsy and are on Antiepileptic Drug (AEDs). Clinical studies have proven the use of AEDs in migraine. Many studies have found that migraine occurs together with other comorbidities like epilepsy. Treatment of both the disorders includes drugs which reduce the CNS transmission though the mechanism may be different in either of the disease.

Aims & Objectives: 1. To study the frequency of migraine in patients with new onset epilepsy.

2. To study the effect of various AEDs on frequency, severity, pattern and disability in patients of migraine.

Material & Methods: This study will be conducted in the new onset epilepsy patients with headache, attending neurology OPD and epilepsy clinic. Patients will be started on monotherapy of AEDs and after the stable dose of monotherapy (3 months) follow up will be done for 3 months. Patients with non epileptic seizures and those who are on polytherapy will be excluded. The data from each patient will be entered on a preformed Performa. Relationship of antiepileptic drugs with migraine in terms of severity, frequency, pattern and disability will be assessed on VAS and GAMS scale over a period of 3 months.

Clinical Significance: This study will help to assess the effect of the Antiepileptic drugs on Migraine.

Keywords: Epilepsy, Migraine, AEDs, Migraine Dairy, GAMS Scale, VAS Scale.

(Signature)	(Signature)	(Signature)	(Signature)	(Signature)
Candidate	Co-supervisor	Co- supervisor	Supervisor	Principal

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis entitled "**TO STUDY THE EFFECT OF ANTIEPILEPTIC DRUGS ON MIGRAINE IN PATIENTS WITH NEW ONSET EPILEPSY**" exist in the Department of Pharmacology, Dayanand Medical College & Hospital, Ludhiana and will be provided to the candidate. We will see that the data being included in the thesis are genuine and is collected by the candidate herself under our supervision and guidance.

Supervisors

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APPROVAL PROFORMA
BY RESEARCH & ETHICAL COMMITTEE
DAYANAND MEDICAL COLLEGE & HOSPITAL, LUDHIANA

Name of candidate	Dr. Samriti Jain
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Likely date of appearing in PG examination	May - 2022
Date of enrolment	10-May-2019
Name of Head of Department	Dr. Sandeep Kaushal
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Dr. Jaspal Singh (Professor & Head, Surgery)	Mr. A K Jindal (Member, Ethics Committee)
Dr. Dinesh Gupta (Professor & Head, Medicine)	Dr. Anu Sharma (Professor, Anatomy)
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Approved: Yes / ~~No~~

Dr. Sandeep Puri
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Prof. Arvind Malhotra
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PERFORMA FOR REGISTRATION OF SUBJECTS FOR DISSERTATION

1	NAME OF THE CANDIDATE AND ADDRESS	Dr. Samriti Jain Mohalla nasirpurian, Near sadar bazar, Sultanpur lodhi. Dist. Kapurthala
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4	DATE OF ADMISSION OF COURSE	10-May-2019
5	TITLE OF THE TOPIC	TO STUDY THE EFFECT OF ANTIEPILEPTIC DRUGS ON MIGRAINE IN PATIENTS WITH NEW ONSET EPILEPSY

6. BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR THE STUDY

Epilepsy is the most common neuronal disorder after stroke and is characterized by presence of recurrent seizures due to chronic underlying process. The incidence of epilepsy is ~0.3–0.5% in different populations throughout the world, and the prevalence of epilepsy has been estimated at 5–30 persons per 1000.[1]

Majority of the people with epilepsy are treated with antiepileptic drugs (AEDs) and approximately 70% undergo remission once the most effective regimen is followed.[2] AEDs differ in the type and severity of adverse drug reaction (ADR), mostly during initiation and early treatment. AEDs are known to have additional effects in comorbidities mainly migraine, neuropathic pain etc [3] along with the spectrum of ADRs. Headache is under-recognized in patients with epilepsy and as a result it is often under-treated. Worldwide, about 46% of population has active headache disorder. Migraine represents about 11% among them.[4]

Migraine is characterized by recurrent headaches and other neurological symptoms. Studies have found that migraine occurs along with other co-morbidities like epilepsy, stroke, sub-clinical vascular brain lesions, coronary heart disease, hypertension etc.[5] There is a new term Migralepsy, with only a few cases described in the literature.[6] The International Headache Society proposed International Classification for Headache Disorders (ICHD-3) which states that the following diagnostic criteria should be met:

Diagnostic criteria: [7]

A. A seizure fulfilling diagnostic criteria for one type of epileptic attack, and criterion B below
B. Occurring in a patient with 1.2 Migraine with aura, and during or within 1 hour after an attack of migraine with aura
C. Not better accounted for by another ICHD-3 diagnosis.

Studies have proved the use of AEDs in prophylaxis of Migraine and also show the reduction in headache frequency in known cases of migraine with epilepsy.[8] The treatment for both disorders includes drugs which reduce the CNS transmission, though the mechanism may differ in either of disease.

The co morbidity headaches in epilepsy is controversial despite the evidence, as a result continued effort is required to increase awareness in the healthcare community.[4]

The study is being planned to evaluate the frequency, severity, disability and pattern of migraine headache in patients with epilepsy and migraine and effects of AEDs in patients attending epilepsy or neurology clinics in a tertiary care hospital of Ludhiana.

6.2 REVIEW OF LITERATURE

Epilepsy is characterized by unprovoked seizures that require long term or lifelong therapy. Seizures are behavioural changes that result from abnormal, paroxysmal neuronal discharges that represent a symptom of underlying brain problem.[9] This has been defined as a sudden and self-limited clinical event that results from abnormal and excessive firing of cortical neurons. Seizures may result from acute head trauma, alcohol withdrawal or hypocalcaemia. The International League Against Epilepsy has given a definition of epilepsy according to which the various elements are-

1. History of at least one seizure
2. Alterations in brain that increase the chances of future seizures.
3. Associated cognitive, neurobiologic, social and psychological disturbances.[10]

There are different types of epilepsy and choice of AEDs depends upon etiology, semiology of epilepsy and other patient related factors.

Classification of Epileptic Seizures[11]		
Seizure Type	**Conventional Anti-Seizure Drugs**	**Recently Developed Anti-Seizure Drugs**
Partial Seizures		
Focal Aware	Carbamazepine, phenytoin, valproate	Brivarscetam, eslicarbazepine, ezogabine, gabapentin, lacosamide, lamotrigine, levetiracetam, perampenal, rufinamide, tiagabine, topiramate, zonisamide
Focal with Impaired awareness	Carbamazepine, phenytoin, valproate	Brivarscetam, eslicarbazepine, ezogabine, gabapentin, lacosamide, lamotrigine, levetiracetam, perampenal, rufinamide, tiagabine, topiramate, zonisamide

Classification of Epileptic Seizures[11]		
Seizure Type	**Conventional Anti-Seizure Drugs**	**Recently Developed Anti-Seizure Drugs**
Partial Seizures		
Focal to bilateral tonic-clonic	Carbamazepine, phenobarbital, phenytoin, primidone, valproate	Brivarscetam, eslicarbazepine, ezogabine, gabapentin, lacosamide, lamotrigine, levetiracetam, perampenal, rufinamide, tiagabine, topiramate, zonisamide
Generalized Seizures		
Absence seizure	Ethosuximide, valproate, clonazepam	Lamotrigine
Myoclonic seizure	Valproate, clonazepam	Levetiracetam
Tonic-clonic seizure	Carbamazepine, phenobarbital, phenytoin, primidone, valproate	Lamotrigine, levetiracetam, topiramate

Anti epileptic drugs

The first antiepileptic drug to be discovered was bromide, followed by Phenobarbital (PB) that was the first synthetic organic agent found to have antiseizure activity.[12] Merritt and Putnam, who developed the electroshock seizure test in experimental animals, discovered the ability of diphenylhydantoin to suppress seizure without causing sedation.[13] The chemical structure of the drugs introduced before 1965 resembled PB and included hydantoins and succinimides. This was followed by development of iminostilbines (carbamazepines), branched chain carboxylic acid (valproic acid) and more recently phenyltriazines (lamotrigine), cyclic analogue of GABA (gabapentin),

sulfamate substituted monosacchride (topiramate), nipecotic acid derivatives (tiagabine) and pyrrolidine derivative (levetiracetam).[13]

Mode of action of antiepileptic drugs [14]

1. Inhibition of sodium currents – by conventional antiepileptics like carbamazepine, phenobarbital, phenytoin, valproate
2. Enhance GABA-ergic inhibition - by novel antiepileptic drugs like tiagabine and vigabatrin.
3. Inhibition of excitatory neurotransmitters e.g. Glutamate
4. Decreasing influx of calcium ions into neurons via a specific subunit of voltage-dependent calcium channels e.g eslicarbazepine, lamotrigine

Newer Antiepileptic Drugs

Compared to traditional AEDs long term administration of new AEDs elicits fewer ADR, fewer drug interactions and teratogenicity. These characteristics increase drug compliance although the antiepileptic effects of the new AEDs are not greater than of traditional AEDs[5]

Newer AEDs have several ADR which vary from mild to life-threatening, and many studies have been conducted to compare AEDs on basis of their CNS, psychiatric or other general ADR.[8]

Patients are often not aware of mood and cognitive changes. Family members are often more aware of behaviour changes than the patient. Mood disorders, mainly anxiety and depression, are common comorbidities in epilepsy.[15]

ADR differ in severity depending upon different AEDs, mostly occur during early or initial phase of the treatment. Some are related to pharmacodynamic, often affected by the dose and rate of initiation, while other concerns are peculiar to the drug. Thus, common reason for changing medication is lack of tolerability. Although ADR can occur with all AEDs, and CNS effects are most common.[15] AEDs have many ADR, and many studies have compared AEDs based on their CNS psychiatric or general medical ADR. Most of the studies consider CNS-related ADR as the main ADR in topiramate (TPM), oxcarbazepine (OXC), and zonisamide (ZNS) consumption.[8]

Behavioural side effects can occur with levetiracetam (LEV), as well as with TPM, ZNS and PB. Irritability and hostility are the main concerns with LEV, often seen soon after initiation. It was reported on a study of 629 patients who were given LEV to compare its effects on older versus younger adults: 31.7% of younger and 40.7% of older patients reported intolerability to LEV on at least one occasion. In both age groups, psychiatric and behavioural side effect were the most common ADR associated with LEV.[16]

Migraine headache afflicts 10-20% of the population. Although it is a specific neurological syndrome, the manifestations vary widely. The principle types and migraine with aura, migraine without aura and several other rare types. It can be unilateral or bilateral. It is a widespread pathology in both epileptics and non-epileptics. Attack can be so severe that it can lead to disability in the patient. However studies have shown reduction in headache frequency in known cases of migraine with epilepsy.

ICHD 3 Criteria for Migraine [7]

1. Migraine
   - 1.1 Migraine without aura
   - 1.2 Migraine with aura
     - 1.2.1 Migraine with typical aura
       - 1.2.1.1 Typical aura with headache
       - 1.2.1.2 Typical aura without headache
     - 1.2.2 Migraine with brainstem aura
     - 1.2.3 Hemiplegic migraine
       - 1.2.3.1 Familial hemiplegic migraine (FHM)
         - 1.2.3.1.1 Familial hemiplegic migraine type 1 (FHM1)
         - 1.2.3.1.2 Familial hemiplegic migraine type 2 (FHM2)
         - 1.2.3.1.3 Familial hemiplegic migraine type 3 (FHM3)
         - 1.2.3.1.4 Familial hemiplegic migraine, other loci
       - 1.2.3.2 Sporadic hemiplegic migraine (SHM)
     - 1.2.4 Retinal migraine
   - 1.3 Chronic migraine
   - 1.4 Complications of migraine

1.4.1 Status migrainosus

1.4.2 Persistent aura without infarction

1.4.3 Migrainous infarction

1.4.4 Migraine aura-triggered seizure

1.5 Probable migraine

1.5.1 Probable migraine without aura

1.5.2 Probable migraine with aura

1.6 Episodic syndromes that may be associated with migraine

1.6.1 Recurrent gastrointestinal disturbance

1.6.1.1 Cyclical vomiting syndrome

1.6.1.2 Abdominal migraine

1.6.2 Benign paroxysmal vertigo

1.6.3 Benign paroxysmal torticollis

Drugs used for prophylaxis of migraine[17] :-

- Angiotensin II blockers-Candesartan
- Anti-convulsants
  - Sodium valproate
  - Topiramate
  - Gabapentin
- Anti-serotonergic (Anti 5-HT) drugs
  - Pizotifen
  - Methysergide
- Beta-blockers
  - Propranolol
  - Metoprolol
  - Atenolol
  - Nadolol
  - Timolol
- Calcitonin Gene-Related Peptide pathway monoclonal antibodies
- Calcium channel blockers
  - Flunarizine
- Non-steroidal anti-inflammatory drug (NSAIDs)

- Naproxen
- Tricyclic antidepressants (TCAs)
  - Amitriptyline
  - Dosulepin
  - Nortriptyline

For acute attack

- Nonspecific Abortive Migraine Therapy
  - NSAIDs –Aspirin, Ibuprofen
- Migraine specific medications
  - Triptans – Sumatriptan,Rizatriptan
  - Ergotamine derivatives-Ergotamine,Dihydroergotamne

Clinical studies on role of Antiepileptic drugs in Migraine

Headache is under-recognized in patients with epilepsy and as a result, it is often under-treated. Around 7%-57% of patient with epilepsy (PWE) are reported to have active interictal headaches, among them Migraine is seen in 2%-26.3% of population.[5]

Prospective, double-blind, placebo-controlled clinical trials of Divalproex and Gabapentin for migraine prevention were done in 2001. The important efficacy variable was a decrease in the 28-day frequency of migraine headache. It was observed that those who received divalproex for 12 weeks at doses up to 1500 mg/day achieved significant decreases in the migraine frequency which were also observed with gabapentin (1800 to 2400 mg/day) when compared with placebo, and half among the patients who were treated with highest dose experienced a reduction in headache rate of 50% or more.[18]

Another placebo-controlled, double-blind parallel group study of 69 patients randomized to LEV 1000 mg/day, TPM 100 mg/day, or placebo, showed that patients were likely to experience a ≥ 50% reduction in headache frequency with LEV as compared with placebo. There was a small but significant difference favouring the efficacy of TPM.[3] Similarly, another study of 85 patients randomized to LEV 500 mg/day, valproate (VPA) 500 mg/day, or placebo, showed 50% decrease in headache frequency in the LEV group compared with the

placebo, with no statistical difference in improvement between LEV and VPA. Small-scale trials and conflicting evidence showed the need for large-scale studies to establish evidence for LEV's use in migraine prevention.[3]

There is conflicting evidence regarding the use of oral LEV for migraine prevention. A 2011 placebo-controlled, crossover trial found 3000 mg of LEV had not produced a significant reduction in migraine frequency. However, researchers did show a trend toward decreased head pain severity, disability and frequency with LEV. Whereas a prospective randomized placebo-controlled study of 52 patients showed LEV at lower dose resulted in a lower headache rate as compared with placebo. However, this trial had limitations.[3]

The association of migraine as common co morbidity in epilepsy is controversial despite their being a reported reduction of attacks of migraine with AEDs. As a result, continued effort is required to increase awareness in the healthcare community.[5]

The study has been planned to evaluate the effect of AEDs on frequency, severity, disability and pattern of migraine headache. Patients with epilepsy and migraine attending epilepsy or neurology clinics in a tertiary care hospital will be enrolled and effects of AEDs on the above mentioned parameters (frequency, severity, disability and pattern) will be studied so as to obtain more data. In this study only the Patient with new onset epilepsy along with migraine who has been started on monotherapy will be included.

6.3 AIMS AND OBJECTIVES OF THE STUDY

1. To study the frequency of migraine in patients with new onset epilepsy.
2. To study the effect of various AEDs on frequency, severity, pattern and disability in patients of migraine.

7. MATERIALS AND METHODS

7.1 SOURCE OF DATA

The study will be conducted on patients attending outpatient department of epilepsy and neurology clinic of Dayanand Medical College and Hospital, Ludhiana; they should be on AEDs monotherapy on stable dose i.e. for 3 months.

7.2 METHOD OF COLLECTION OF DATA

Patients with new onset epilepsy and migraine who fulfil the following inclusion and none of the exclusion criteria will be included in the study.

INCLUSION CRITERIA

1. Age- 18 to 65 years
2. Gender- either
3. Semiology- any
4. Patient on Monotherapy (Any AED) on a stable dose for 3 months.

EXCLUSION CRITERIA

1. Non consenting individual
2. Patients on stable AED dose <3 months
3. Patients on polytherapy
4. Known case of epilepsy

Patients who fulfil the following diagnostic criteria will be considered as having Migraine headache:-

Diagnostic Criteria for Migraine [19]

Repeated attacks of headache lasting 4–72 h in patients with a normal physical examination, no other reasonable cause for the headache, and:

At least 2 of the following features:

1. Unilateral pain
2. Throbbing pain
3. Aggravation by movement
4. Moderate or severe intensity

Plus at least 1 of the following features:

1. Nausea/vomiting
2. Photophobia and Phonophobia

They will be evaluated completely regarding the migraine attack and its association with the AEDs. Relationship of AEDs and migraine will be assessed by taking a complete history about the concomitant epilepsy and migraine medications being used. All the data (patients demographics, socioeconomic status using Modified Kuppuswamy scale)[20] will be recorded on the prestructured proforma. Assessment of severity of pain will be done by GAMS[21] and VAS Scale.[22,23]

STUDY DESIGN

This will be a follow-up observational study in which the newly diagnosed patients of epilepsy with migraine will be enrolled. They will be started on the monotherapy with antiepileptic drug (as per choice of neurologist). Assessment will be done over 3 months after stable dose of AED reached. Patient demographics along with clinical characteristics such as seizures semiology, type of migraine (severity, disability, frequency and pattern) along with the complete details of the AED being used by the patient will be recorded. A complete drug history will also be recorded. Along with this they will be asked to maintain a migraine diary[24] which will be collected back at each subsequent visits. Need for the rescue medication – NSAIDs, Triptans or ergot derivatives (dose, frequency) will be asked and recorded. Follow up study will be done for 3 months on monthly basis. They will be interviewed for information regarding migraine history.

Global assessment of migraine severity (GAMS) scale.[21]

For assessing the severity of the pain we will be using the **Global assessment of migraine severity (GAMS) scale**. In this the severity of the pain will be obtained by asking the patient to respond to a single question: "Taking into account all aspects of your disease, how severe is your disease?" And the answer will have seven response categories

(1) Not at all severe

(2) A little severe

(3) Somewhat severe

(4) Moderately severe

(5) Quite severe

(6) Very severe

(7) Extremely severe

This single severity question will measures the overall severity since migraine onset. This format of GAMS and the choice of response were based on the previously validated Global Assessment of Severity in Epilepsy (GASE) which is being widely used to measure the severity in epilepsy

Visual Analogue scale (VAS) [22,23]

Another scale we will be using for assessment of pain is **Visual Analogue scale (VAS).** In this we will measure the two aspects-

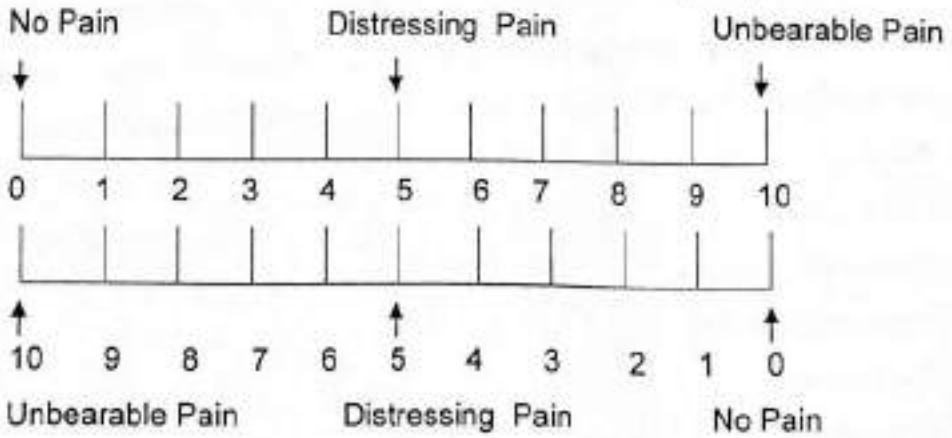
1. The intensity of the headache i.e. How strong the pain feels?
2. The unpleasantness associated with the headache i.e. How disturbing the pain is?

VAS is easy to understand and administer to the patients. It is valid method for measuring the above two aspects. This scale has the vertical line which is anchored by the statement that represents the extremes of the aspects we want to measure. For example on one extreme of the vertical line there will be "The most nervous I have ever been" and on the other extreme there will be "Not nervous at all", the subject will be asked to place the line across the scale at the point which represent the intensity of the pain at that give time. This will help us to measure the intensity of the pain patient is feeling at that particular moment.

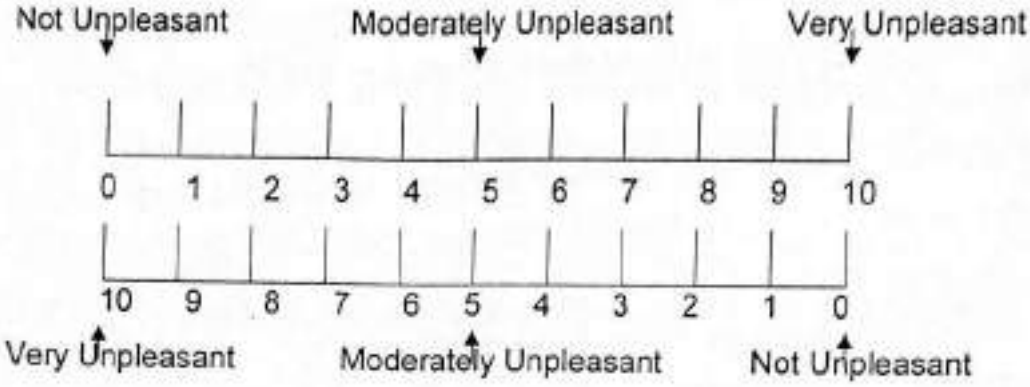
In the same way patient will be asked to place a line across another VAS for the unpleasantness of the headache.

Visual Analogue Scale-

Choose a number from 0 to 10 that best describe your pain



Choose a number from 10 to 0 that best describe the unpleasantness of the headache


Not Unpleasant
Moderately Unpleasant
Very Unpleasant
0 1 2 3 4 5 6 7 8 9 10
10 9 8 7 6 5 4 3 2 1 0
Very Unpleasant
Moderately Unpleasant
Not Unpleasant

DURATION OF STUDY

Enrolment- 1 Year

Follow up- 3 Months

OUTCOME PARAMETERS

1. Assessment of improvement or worsening of migraine in terms of frequency, pattern, severity and disability in patient on AEDs.
2. Any change in pattern of migraine and need for acute treatment (rescue).

STATISTICAL ANALYSIS

Data will be described in terms of range; mean ± standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. All statistical calculations will be done using SPSS (Statistical Package for the Social Science) SPSS 21 version statistical program for Microsoft Windows.

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

No

7.4 ETHICAL CLEARANCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?

Ethical clearance attached along with

8. LIST OF REFERENCES

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DEPARTMENT OF PHARMACOLOGY

DAYANANAD MEDICAL COLLEGE AND HOSPITAL, LUDHIANA

PROFORMA

Date:_____ Sr. No_____

Name :_____ Age/Gender_____Father's/Husband name:_____

Occupation:_____Address:_____

Phone No:_____Socioeconomic status_____

H/o epilepsy:_____ Seizure semiology:_____

Age at onset of epilepsy :_____Frequency of seizures_____/_____

History of migraine- Yes/No Frequency of migraine _____attacks/_____

Age of onset of migraine_____ yrs Triggering factors(if any)_____

Family history of Epilepsy/ diabetes/ hypertension/ asthma,/TB/ Migraine/any other.-

_____

Past history:_____

H/O drug allergy (if any):_____

General Physical Examination (Date-_____)

Height:_____ Weight:_____Anaemia :_____ Jaundice:_____

Cyanosis:_____Oedema:_____ Lymphdenopathy_____

BP:_____mmHg Pulse :_____bpm Respiratory Rate_____/min

Systemic Examination

CNS:_____

CVS :_____

Respiratory_____

Abdomen:_____

Signature of Candidate **Signature of Supervisor**

Drug History

S.no.	Generic name of the drug	Brand name of the drug	Dose	Frequency	Start date	Stop date	ADR (if any)
1							
2							
3							
4							
5							
6							
7							
8							
9							
10							

Types of migraine along with the history of acute attack and medications taken.

S. no.	Type of Migraine	Acute Attack Present		Medication taken (Yes/No)	Dose	Frequency
		Yes (Date)	No			
1	Migraine with aura					
2	Migraine without aura					
3	Hemiplegic migraine					
4	Retinal migraine					
5	Ice pick migraine					
6	Cervicogenic headache					

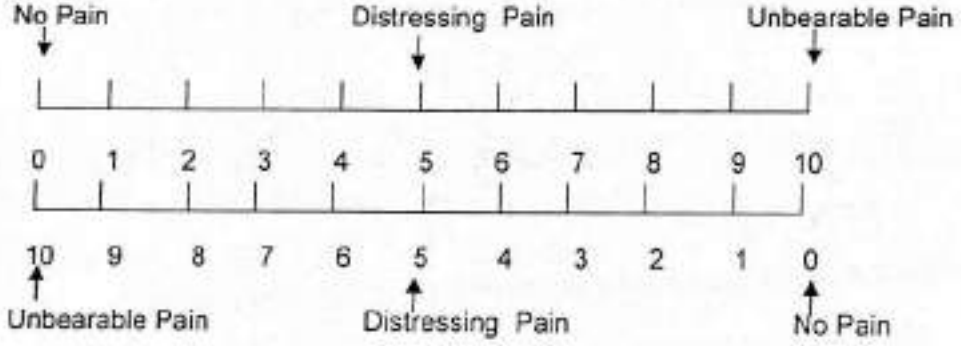
THREE MONTH FOLLOW UP PROFORMA

1st month _____20__

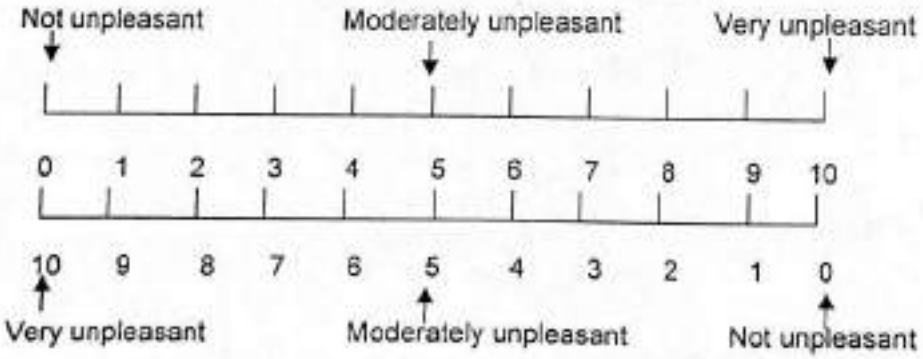
Type of migraine attack	Effect on					
	Frequency (___/month)	Pattern	Severity		Disability	Triggering factor (if any)
			VAS	GAMS		
Migraine with aura						
Migraine without aura						
Hemiplegic migraine						
Retinal migraine						
Ice pick migraine						
Cervicogenic headache						

Severity scales

1. VAS



Choose a number from 10 to 0 that best describe the unpleasantness of the headache


Not unpleasant
Moderately unpleasant
Very unpleasant
0 1 2 3 4 5 6 7 8 9 10
10 9 8 7 6 5 4 3 2 1 0
Very unpleasant
Moderately unpleasant
Not unpleasant

2. GAMS

Q: Taking into account all aspects of your disease, how severe is your disease?

(1) Not at all severe (2) A little severe (3) Somewhat severe

(4) Moderately severe (5) Quite severe (6) Very severe (7) Extremely severe

Signature of Candidate

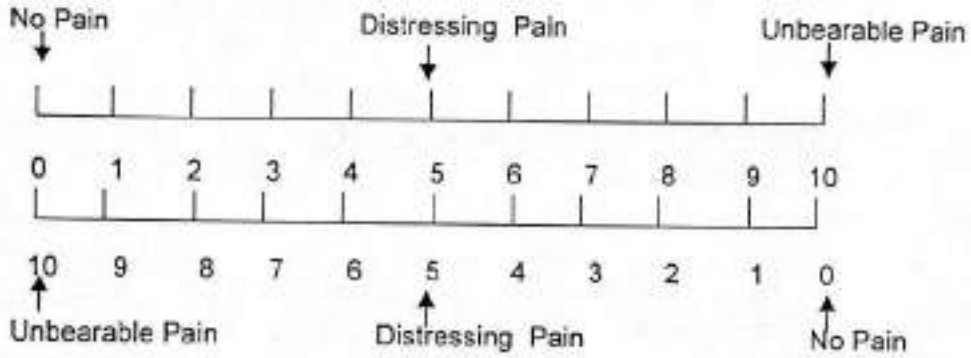
Signature of Supervisor

2nd month _____20__

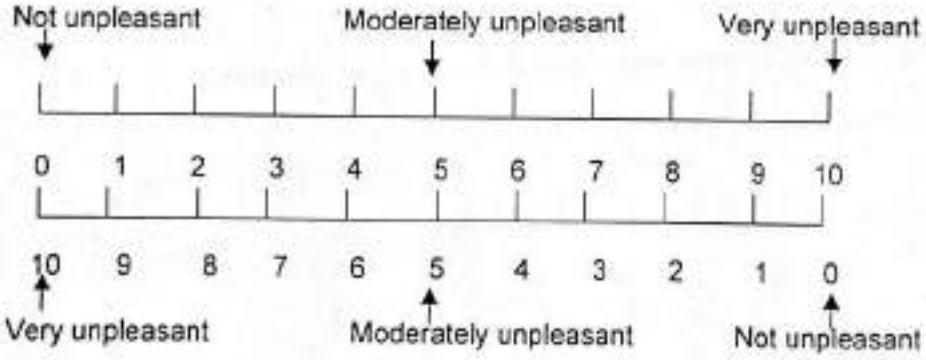
Type of migraine attack	Effect on					
	Frequency (___/month)	Pattern	Severity		Disability	Triggering factor (if any)
			VAS	GAMS		
Migraine with aura						
Migraine without aura						
Hemiplegic migraine						
Retinal migraine						
Ice pick migraine						
Cervicogeric headache						

Severity scales

1. VAS



Choose a number from 10 to 0 that best describe the unpleasantness of the headache


Not unpleasant
Moderately unpleasant
Very unpleasant
0 1 2 3 4 5 6 7 8 9 10
10 9 8 7 6 5 4 3 2 1 0
Very unpleasant
Moderately unpleasant
Not unpleasant

2. GAMS

Q: Taking into account all aspects of your disease, how severe is your disease?

(1) Not at all severe (2) A little severe (3) Somewhat severe

(4) Moderately severe (5) Quite severe (6) Very severe (7) Extremely severe

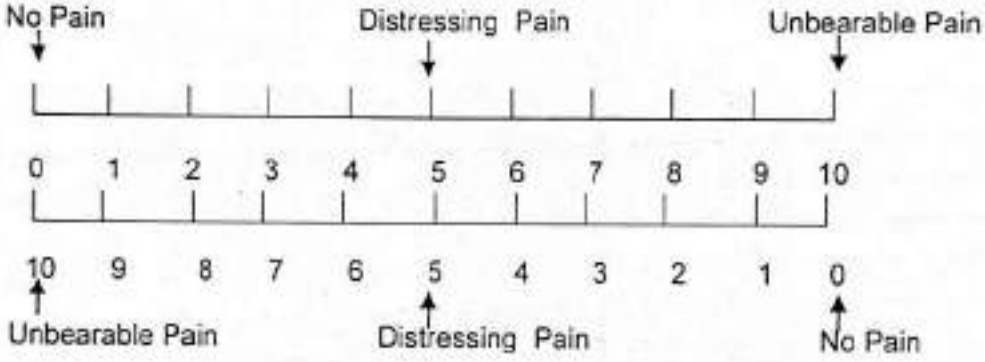
Signature of Candidate **Signature of Supervisor**

3rd month _____20__

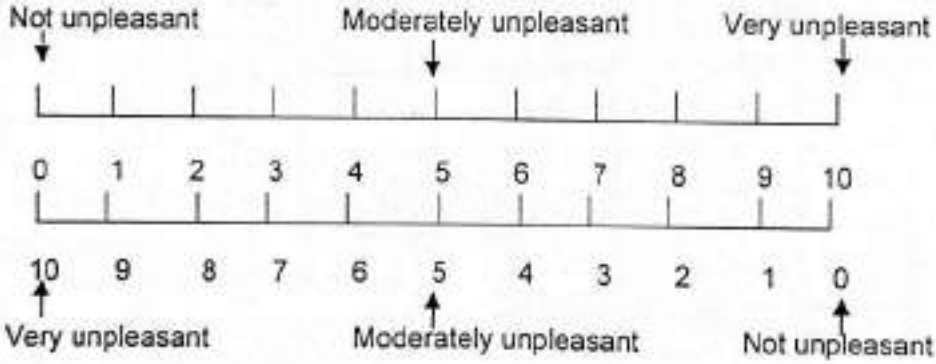
Type of migraine attack	Effect on					
	Frequency (___/month)	Pattern	Severity		Disability	Triggering factor (if any)
			VAS	GAMS		
Migraine with aura						
Migraine without aura						
Hemiplegic migraine						
Retinal migraine						
Ice pick migraine						
Cervicogenic headache						

Severity scales

1. VAS



Choose a number from 10 to 0 that best describe the unpleasantness of the headache


Not unpleasant
Moderately unpleasant
Very unpleasant
0 1 2 3 4 5 6 7 8 9 10
10 9 8 7 6 5 4 3 2 1 0
Very unpleasant
Moderately unpleasant
Not unpleasant

2. GAMS

Q: Taking into account all aspects of your disease, how severe is your disease?

(1) Not at all severe (2) A little severe (3) Somewhat severe

(4) Moderately severe (5) Quite severe (6) Very severe (7) Extremely severe

Signature of Candidate

Signature of Supervisor

Migraine dairy _____20__

Date (Month)	Time (start/ finish)	Intensity Rate 1-10 (most severe being 10)	Preceding symptoms	Triggers	Medications (and dosage)	Relief (complete/ moderate/ none)
1						
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
13						
14						
15						
16						
17						
18						
19						
20						
21						
22						
23						
24						
25						
26						
27						
28						
29						
30						
31						

Signature of Candidate

Signature of Supervisor

DEPARTMENT OF PHARMACOLOGY, DAYANANAD MEDICAL COLLEGE AND HOSPITAL, LUDHIANA

Interview Questionnaire[4]

1. Have you had at least one episode of head or facial pain in the last 12 months?

   Yes ☐ No ☐

2. On average, in the last three months, how many days per month have you had head or facial pain? _____days

3. Can your head pain occur more than once per day? Yes ☐ No ☐

3a If yes, on average, how many attacks per day?_____

4. How long does each attack of head or facial pain last if untreated or unsuccessfully treated (please label as either minutes or hours)? _____

5. At the onset of the head or facial pain is the pain on one side (unilateral) or both sides (bilateral)? Unilateral ☐ Bilateral ☐

5a. If Unilateral, is the pain always on the same side? Yes ☐ No ☐

6. Where is your pain located? (Pick all that apply)
   a) Around the eye
   b) Temple
   c) Back of the head
   d) Side of the head
   e) Other(please describe)

6a.Please describe the location of your head or facial pain if you selected "other" for the previous question_____

7. Which of the following describes your pain in the best?
   a) Pressing/lightening
   b) Throbbing/Pulsating
   c) Stabbing
   d) Burning
   e) Other(please describe)

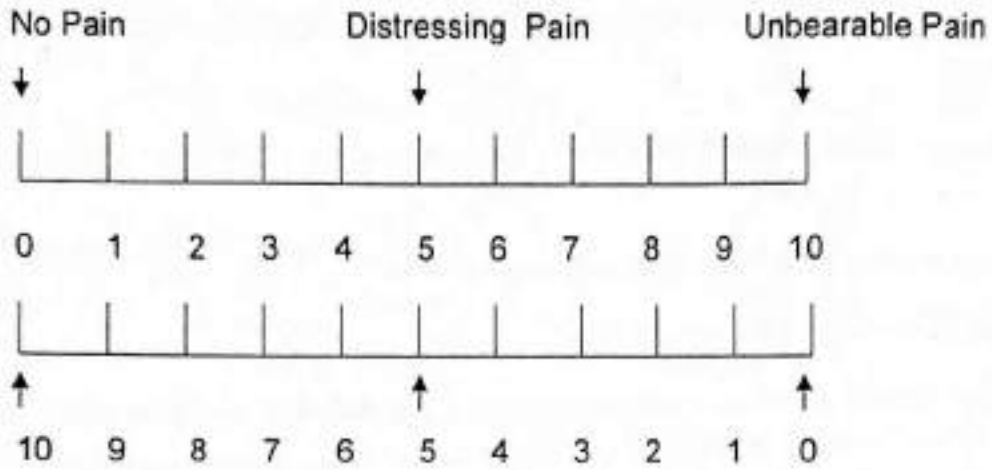
7a.Please describe your pain if you selected "other" for the previous question:

_____

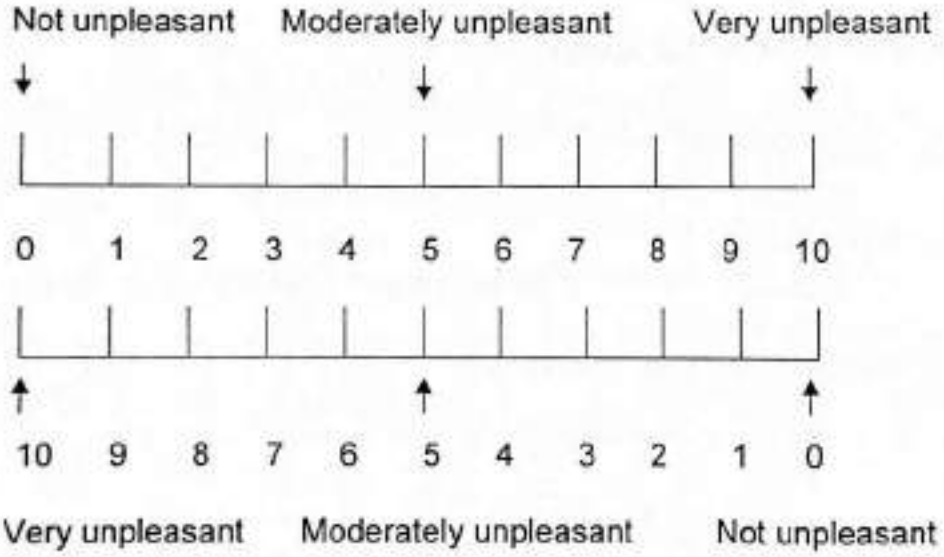
8.What is the intensity of your pain ,an average rated on a scale of 0 (no pain) to 10 (worst pain ever)?

Visual Analogue Scale-

Choose a number from 0 to 10 that best describe your pain



Choose a number from 10 to 0 that best describe the unpleasantness of the headache


Not unpleasant
Moderately unpleasant
Very unpleasant
0 1 2 3 4 5 6 7 8 9 10
10 9 8 7 6 5 4 3 2 1 0
Very unpleasant
Moderately unpleasant
Not unpleasant

9.Check any of the following symptoms that you experience frequently along with your headache (Pick all that apply):

a) Nausea or sick to your stomach
b) Sensitivity to light
c) Sensitivity to sound
d) Eye redness
e) Tearing
f) Nasal congestion
g) Eye drooping
h) Running nose

i) Eyelid swelling
j) Facial and forehead sweating
k) Sense of agitation

9a. If any of the above occur on one side ,do they occur on the same side as the headache

Yes ☐ No ☐

10.Does the head or facial pain get worse due to or lead to avoidance of physical activity?

Yes ☐ No ☐

11.Do you have any fully reversible neurologic symptom(s) before the onset of your head or facial pain? Yes ☐ No ☐

11a.Which of the followings describes the neurologic symptom(s) best (may tick >1)?
a) Visual symptoms on one side
b) Sensory (i.e. Numbness or tingling) symptoms on one side
c) Speech disturbance
d) Weakness on one side
e) Other

11a* Please describe the neurologic symptom(s) if you checked "other" in the previous question_____

11b) How long do the neurologic symptom(s) last (Choose one)
a) Less than 5 minutes
b) 5 to less than 60 minutes
c) 60 minutes to less 24 hours
d) 24 hours or more

12. Are there factors that may worsen an existing attack of head or facial pain (if yes, please describe)_____

13. Are there any factors that can bring on (trigger) an episode of head or facial pain (if yes, please describe)?_____

14. Can any of the following bring on an attack of head or facial pain(may check more than one) ?
a) Cough
b) Straining for a bowel movement
c) Lying flat
d) Moving from lying flat to an upright position
e) None of the above

15. Please list any medications you have attempted to relieve an acute attack of head or facial pain (Please include dose, effect on pain and any side effects):

_____

16.Please list any daily medications you have tried to prevent or lessen the frequency of you head or facial pain: _____

Modified Kuppuswamy scale (2019)[24]

Education of head of family	Score
Professional degree	7
Graduate or postgraduate	6
Intermediate or post high school diploma	5
High school certificate	4
Middle school certificate	3
Primary school certificate	2
Illiterate	1
Occupation of head of family	
Professional (white collar)	10
Semi-professional	6
Clerical, shop-owner/farm	5
Skilled worker	4
Semi-skilled worker	3
Unskilled worker	2
Unemployed	1

In 2019 (February 2019 CPI)	Score
≥52,734	12
26,355-52,733	10
19,759-26,354	6
13,161-19,758	4
7,887-13,160	3
2,641-7,886	2
≤2,640	1

Socioeconomic class		Total score
I	Upper	26-29
II	Upper middle	16-25
III	Lower middle	11-15
IV	Upper lower	5-10
V	Lower	01-04

INFORMED PATIENT CONSENT

Date: _____

I.....D/o, W/o, S/o..... .....am willing to participate in the study **"TO STUDY THE EFFECT OF ANTIEPILEPTIC DRUGS ON MIGRAINE IN PATIENTS WITH NEW ONSET EPILEPSY"** The procedure with its complications has been explained to me in local vernacular language. I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out the study any time without assigning any reason.

....

Signature of the Witness Signature of the patient

Name:

Signature of Candidate **Signature of Supervisor**

मरीज अनुमति फार्म

तिथि _____

मैं _____ पत्नी/पुत्र/पुत्री _____

निवासी _____

इस शोधकार्य "TO STUDY THE EFFECT OF ANTIEPILEPTIC DRUGS ON MIGRAINE IN PATIENTS WITH NEW ONSET EPILEPSY" में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ की यह स्वीकृति देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है की यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामुली है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे इलाज पर कोई प्रभाव नहीं पड़ेगा।

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गवाह के हस्ताक्षर

नाम:

_____

रोगी के हस्ताक्षर/अंगूठे का निशान

नाम:

_____

अन्वेषक के हस्ताक्षर

_____

विद्यार्थी के हस्ताक्षर

ਮਰੀਜ਼ ਰਜ਼ਾਮੰਦੀ ਫਾਰਮ

ਮਿਤੀ_____

ਮੈ_____ਪਤਨੀ/ਪੁੱਤਰ/ਪੁੱਤਰੀ_____

ਵਾਸੀ _____

"TO STUDY THE EFFECT OF ANTIEPILEPTIC DRUGS ON MIGRAINE IN PATIENTS WITH NEW ONSET EPILEPSY" ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ ਹਾਂ/ ਚਾਹੁੰਦੀ ਹਾਂ ਕੇ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂ ਕਿਸੇ ਵੀ ਤਰਾਂ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ – ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।

ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

_____ _____

ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____ ਮਿਤੀ_____

ਪਤਾ _____ ਪਤਾ _____

_____

ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

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ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ